WEST Search History

DATE: Wednesday, July 10, 2002

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR			
L12	L11 and @ad<19960523	7	L12
L11	L9 and (class adj II)	79	L11
L10	L9 and (class II)	92	L10
L9	L8 and (MHC)	92	L9
L8	((CD80 or B7.1) same(ICAM$2 or CD54 or CD50 or CD102)) and (CD4 or CD4+)	107	L8
L7	(CD80 or B7.1) same(ICAM$2 or CD54 or CD50 or CD102)	152	L7
L6	(CD80 or B7.1) and (ICAM$2 or CD54 or CD50 or CD102)	254	L6
L5	L4 and (ICAM$2 or CD54 or CD50 or CD102)	5	L5
L4	L3 and ((CD80 or B7.1))	5	L4
L3	L2 and CD4$2	60	L3
L2	(webb)[IN] OR (wingvist)[IN] or(karlsson) [in] or (Jackson) [in] or (peterson)[in]	33315	L2
L1	(webb)[IN] OR (wingvist)[IN]	5841	L1

END OF SEARCH HISTORY

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=> dis his

     (FILE 'HOME' ENTERED AT 10:03:54 ON 10 JUL 2002)

     FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 10:04:06 ON 10 JUL 2002
L1         14884 S WEBB S?/AU OR WINGVIST O?/AU OR KARLSSON L?/AU OR JACKSON M?/
L2           198 S L1 AND CD4?
L3           185 S L2 NOT CD40
L4            14 S L2 AND (CD80 OR B7.1)
L5             7 DUP REM L4 (7 DUPLICATES REMOVED)
L6             5 S L5 AND (ICAM? OR CD54 OR CD50 OR CD102)
L7        233993 S CD4?
L8        217789 S L7 NOT CD40
L9          2210 S L8 AND (CD80 OR B7.1)
L10          322 S L9 AND (ICAM? OR CD54 OR CD50 OR CD102)
L11           72 S L10 AND PD<19960523
L12           34 DUP REM L11 (38 DUPLICATES REMOVED)
L13           15 S L12 AND HIS?
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09/715,231

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 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  Jan 25  BLAST(R) searching in REGISTRY available in STN on the Web
 NEWS  3  Jan 29  FSTA has been reloaded and moves to weekly updates
 NEWS  4  Feb 01  DKILIT now produced by FIZ Karlsruhe and has a new update
                  frequency
 NEWS  5  Feb 19  Access via Tymnet and SprintNet Eliminated Effective 3/31/02
 NEWS  6  Mar 08  Gene Names now available in BIOSIS
 NEWS  7  Mar 22  TOXLIT no longer available
 NEWS  8  Mar 22  TRCTHERMO no longer available
 NEWS  9  Mar 28  US Provisional Priorities searched with P in CA/CAplus
                  and USPATFULL
 NEWS 10  Mar 28  LIPINSKI/CALC added for property searching in REGISTRY
 NEWS 11  Apr 02  PAPERCHEM no longer available on STN.  Use PAPERCHEM2 instead.
 NEWS 12  Apr 08  "Ask CAS" for self-help around the clock
 NEWS 13  Apr 09  BEILSTEIN: Reload and Implementation of a New Subject Area
 NEWS 14  Apr 09  ZDB will be removed from STN
 NEWS 15  Apr 19  US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
 NEWS 16  Apr 22  Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
 NEWS 17  Apr 22  BIOSIS Gene Names now available in TOXCENTER
 NEWS 18  Apr 22  Federal Research in Progress (FEDRIP) now available
 NEWS 19  Jun 03  New e-mail delivery for search results now available
 NEWS 20  Jun 10  MEDLINE Reload
 NEWS 21  Jun 10  PCTFULL has been reloaded
 NEWS 22  Jul 02  FOREGE no longer contains STANDARDS file segment

 NEWS EXPRESS  February 1 CURRENT WINDOWS VERSION IS V6.0d,
               CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
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FILE 'HOME' ENTERED AT 10:03:54 ON 10 JUL 2002

=>  file medline caplus embase biosis
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                 0.21       0.21

FILE 'MEDLINE' ENTERED AT 10:04:06 ON 10 JUL 2002

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=> s webb S?/au or Wingvist O?/au or Karlsson L?/au or jackson M?/au or Peterson P?/au
L1       14884 WEBB S?/AU OR WINGVIST O?/AU OR KARLSSON L?/AU OR JACKSON M?/AU
               OR PETERSON P?/AU

=> s l1 and CD?
The arrow (=>) is the system prompt, where you enter a command.  For
an explanation of system commands, files, formats, etc., enter "HELP"
and the name of the item you want explained at an arrow prompt (=>).
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Enter "HELP" or "?" at a prompt to see an explanation of the options.
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will receive a more detailed explanation of the error and how to
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Automatic help is also available.  When AUHELP is 'ON', you will
automatically receive help following an error message.  For more
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STN Service Centers.  You may also choose to contact the database
representative for the file you are searching, for more detailed help
on database content and search strategy.  For information on how to
contact database representatives for the current file, enter "HELP
DESK" at an arrow prompt (=>).
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```
=> s l1 and CD4?
L2          198 L1 AND CD4?

=> s l1 and (CD4 or CD4+)
'CD4+' NOT VALID HERE
'CD4+' NOT VALID HERE
'CD4+' NOT VALID HERE
'CD4+' NOT VALID HERE

=> s l2 not cd40
L3          185 L2 NOT CD40

=> s s l2 and (CD80 or B7.1)
MISSING OPERATOR S L2
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l2 and (CD80 or B7.1)
L4           14 L2 AND (CD80 OR B7.1)

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5            7 DUP REM L4 (7 DUPLICATES REMOVED)

=> dis l5 1-7 ibib abs kwic

L5   ANSWER 1 OF 7     MEDLINE                          DUPLICATE 1
ACCESSION NUMBER:   2001296822     MEDLINE
DOCUMENT NUMBER:    21270387   PubMed ID: 11376339
TITLE:              A key role for ICAM-1 in generating effector cells
                    mediating inflammatory responses.
AUTHOR:             Camacho S A; Heath W R; Carbone F R; Sarvetnick N; LeBon A;
                    Karlsson L; Peterson P A; Webb S
                    R
CORPORATE SOURCE:   Department of Immunology, IMM4, The Scripps Research
                    Institute, 10550 North Torrey Pines Road, La Jolla, CA
                    92037, USA.
CONTRACT NUMBER:    AI39664 (NIAID)
                    CA25803 (NCI)
                    CA41993 (NCI)
SOURCE:             Nat Immunol, (2001 Jun) 2 (6) 523-9.
                    Journal code: 100941354. ISSN: 1529-2908.
PUB. COUNTRY:       United States
                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200106
ENTRY DATE:         Entered STN: 20010625
                    Last Updated on STN: 20010625
                    Entered Medline: 20010621
AB   We investigated how the accessory molecule interactions encountered during
     T cell priming influence T cell-mediated destruction of insulin-producing
     beta cells and lead to type 1 diabetes. T cell receptor (TCR)-transgenic
     CD4+ T cells were primed under controlled conditions in vitro
     before being adoptively transferred into transgenic recipients expressing
     membrane ovalbumin under the control of the rat insulin promoter
     (RIP-mOVA). During priming, antigen-presenting cell expression of
     B7-1 without intracellular adhesion molecule 1 (ICAM-1)
     led to the generation of effector cells that migrated to the pancreata of
     RIP-mOVA recipients but did not cause diabetes. In contrast, when T cells
     were primed with APCs expressing both B7-1 and ICAM-1,
     pronounced destruction of beta cells and a rapid onset of diabetes were
     observed. Pathogenicity was associated with T cell production of the
     macrophage-attracting chemokines CCL3 and CCL4. Thus, interactions of
     lymphocyte function-associated antigen 1 with ICAM-1 during priming induce
     both qualitative and quantitative alterations in T effector function and
     induce potentially autodestructive responses.
AU   Camacho S A; Heath W R; Carbone F R; Sarvetnick N; LeBon A; Karlsson
     L; Peterson P A; Webb S R
AB   . . . cell priming influence T cell-mediated destruction of
     insulin-producing beta cells and lead to type 1 diabetes. T cell receptor
     (TCR)-transgenic CD4+ T cells were primed under controlled
     conditions in vitro before being adoptively transferred into transgenic
     recipients expressing membrane ovalbumin under the control of the rat
     insulin promoter (RIP-mOVA). During priming, antigen-presenting cell
     expression of B7-1 without intracellular adhesion
     molecule 1 (ICAM-1) led to the generation of effector cells that migrated
     to the pancreata of RIP-mOVA recipients but did not cause diabetes. In
     contrast, when T cells were primed with APCs expressing both B7-
     1 and ICAM-1, pronounced destruction of beta cells and a rapid
     onset of diabetes were observed. Pathogenicity was associated with T.  .
     .
CT   Check Tags: Animal; In Vitro; Support, Non-U.S. Gov't; Support, U.S.
     Gov't, P.H.S.
      Antigen-Presenting Cells: IM, immunology
        Antigens, CD80: ME, metabolism
        CD4-Positive T-Lymphocytes: IM, immunology
      Diabetes Mellitus, Insulin-Dependent: ET, etiology
      Diabetes Mellitus, Insulin-Dependent: IM, immunology
      Diabetes Mellitus, Insulin-Dependent: PA, pathology
     *Inflammation:. . .
CN   0 (Antigens, CD80); 0 (Lymphocyte Function-Associated
     Antigen-1); 0 (Receptors, Antigen, T-Cell)

L5   ANSWER 2 OF 7  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:       2001:419849  CAPLUS
DOCUMENT NUMBER:        136:100954
TITLE:                  Vaccination with glutamic acid decarboxylase plasmid
                        DNA protects mice from spontaneous autoimmune diabetes
                        and B7/CD28 costimulation circumvents that protection
AUTHOR(S):              Balasa, Balaji; Boehm, Bernhard O.; Fortnagel, Anja;
                        Karges, Wolfram; Van Gunst, Kurt; Jung, Nadja;
                        Camacho, Stephanie A.; Webb, Susan R.;
                        Sarvetnick, Nora
CORPORATE SOURCE:       Department of Immunology, The Scripps Research
                        Institute, La Jolla, CA, 92037, USA
SOURCE:                 Clinical Immunology (San Diego, CA, United States)
                        (2001), 99(2), 241-252
                        CODEN: CLIIFY; ISSN: 1521-6616
PUBLISHER:              Academic Press
DOCUMENT TYPE:          Journal
LANGUAGE:               English
```

AB The nonobese diabetic (NOD) mouse develops spontaneous T-cell-dependent autoimmune diabetes. The authors tested here whether vaccination of NOD mice with a plasmid DNA encoding glutamic acid decarboxylase (GAD), an initial target islet antigen of autoimmune T cell repertoire, would modulate their diabetes. Our results showed that vaccination of young or old female NOD mice with the GAD-plasmid DNA, but not control-plasmid DNA, effectively prevented their diabetes, demonstrating that GAD-plasmid DNA vaccination is quite effective in abrogating diabetes even after the development of insulitis. The prevention of diabetes did not follow the induction of immunoregulatory Th2 cells but was dependent upon CD28/B7 costimulation. Our results suggest a potential for treating spontaneous autoimmune diabetes via DNA vaccination with plasmids encoding self-Ag. (c) 2001 Academic Press.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AU Balasa, Balaji; Boehm, Bernhard O.; Fortnagel, Anja; Karges, Wolfram; Van Gunst, Kurt; Jung, Nadja; Camacho, Stephanie A.; **Webb, Susan R.**; Sarvetnick, Nora

IT B cell (lymphocyte)
CD4-positive T cell
CD8-positive T cell
Gene therapy
Signal transduction, biological
(vaccination with glutamic acid decarboxylase plasmid DNA protects mice from spontaneous autoimmune diabetes and B7/CD28 costimulation circumvents that protection)

IT CD28 (antigen)
CD80 (antigen)
CD86 (antigen)
Fas antigen
Interleukin 2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(vaccination with glutamic acid decarboxylase plasmid DNA protects mice from spontaneous autoimmune diabetes and B7/CD28 costimulation circumvents that protection)

L5 ANSWER 3 OF 7 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 1999179008 MEDLINE
DOCUMENT NUMBER: 99179008 PubMed ID: 10077630
TITLE: Intercellular adhesion molecule-1 inhibits interleukin 4 production by naive T cells.
AUTHOR: Luksch C R; Winqvist O; Ozaki M E; **Karlsson L; Jackson M R; Peterson P A; Webb S R**
CORPORATE SOURCE: Department of Immunology, IMM4, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA.
CONTRACT NUMBER: CA25803 (NCI)
CA41993 (NCI)
+
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Mar 16) 96 (6) 3023-8. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990601
Last Updated on STN: 19990601
Entered Medline: 19990520

AB The type of cytokines produced during T cell responses determines susceptibility or resistance to many pathogens and influences the development of autoimmunity and allergy. To define the role of individual accessory molecules in cytokine production during primary immune responses, Drosophila cell lines expressing murine major histocompatibility complex class II molecules with defined combinations of accessory molecules were used to present peptide antigen to naive T cell receptor transgenic T cells. Significantly, expression of **B7**.1 or B7.2 without additional accessory molecules led to very high production of interleukin (IL)-4, which contrasted with minimal IL-4 production elicited by conventional antigen presenting cells (APC). However, coexpression of ICAM-1 and B7 on Drosophila APC induced little IL-4, suggesting an inhibitory role for intercellular adhesion molecule-1 (ICAM-1). In support of this idea, stimulation of T cell receptor transgenic T cells with peptide presented by splenic APC devoid of ICAM-1 (from ICAM-1-deficient mice) led to high IL-4 production. Thus, the level of IL-4 production by naive **CD4**(+) T cells during typical primary responses appears to be controlled, at least in part, by T-APC interactions involving ICAM-1.

AU Luksch C R; Winqvist O; Ozaki M E; **Karlsson L; Jackson M R; Peterson P A; Webb S R**

AB . . . of accessory molecules were used to present peptide antigen to naive T cell receptor transgenic T cells. Significantly, expression of B7.1 or B7.2 without additional accessory molecules led to very high production of interleukin (IL)-4, which contrasted with minimal IL-4 production. . . APC devoid of ICAM-1 (from ICAM-1-deficient mice) led to high IL-4 production. Thus, the level of IL-4 production by naive **CD4**(+) T cells during typical primary responses appears to be controlled, at least in part, by T-APC interactions involving ICAM-1.

CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Antigen Presentation: GE, genetics
Antigen Presentation: IM, immunology
Antigens, CD80: IM, immunology
Cell Line
Drosophila
Gene Expression Regulation: IM, immunology
Intercellular Adhesion Molecule-1: GE, genetics
*Intercellular Adhesion Molecule-1:. . .

CN 0 (Antigens, **CD80**); 0 (Receptors, Antigen, T-Cell)

L5 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:242167 CAPLUS
DOCUMENT NUMBER: 131:72611
TITLE: Autoimmune regulator is expressed in the cells regulating immune tolerance in thymus medulla
AUTHOR(S): Heino, Maarit; **Peterson, Part**; Kudoh, Jun; Nagamine, Kentaro; Lagerstedt, Anssi; Ovod, Vladimir; Ranki, Annamari; Rantala, Immo; Nieminen, Markku; Tuukkanen, Juha; Scott, Hamish S.; Antonarakis, Stylianos E.; Shimizu, Nobuyoshi; Krohn, Kai
CORPORATE SOURCE: Institute of Medical Technology, University of

Tampere, Tampere, Finland
SOURCE: Biochemical and Biophysical Research Communications (1999), 257(3), 821-825
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The AIRE gene (autoimmune regulator), coding for a putative transcriptional regulatory factor, is mutated in autoimmune-polyendocrinopathy-candidiasis ectodermal dystrophy (APECED). We have investigated the expression of the AIRE gene by mRNA in situ hybridization and immunohistochem. in various human tissues. Here we show that AIRE is expressed in distinct cells in thymus medulla, and also in rare cells in lymph node paracortex and medulla, and in spleen and fetal liver, but not in the target organs of autoimmune destruction. Double immunofluorescence studies revealed that in thymus medulla both epithelial (cytokeratin pos.) and non-epithelial cells expressed AIRE. Subcellularly, AIRE was localized in nuclear dots in thymus and lymph node and also in transfected cells. The cellular localization of AIRE and its nuclear localization, compatible with its predicted protein domains, suggest that AIRE may regulate the mechanisms involved in the induction and maintenance of immune tolerance. (c) 1999 Academic Press.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
AU Heino, Maarit; **Peterson, Part**; Kudoh, Jun; Nagamine, Kentaro; Lagerstedt, Anssi; Ovod, Vladimir; Ranki, Annamari; Rantala, Immo; Nieminen, Markku; Tuukkanen, Juha; Scott, Hamish S.; Antonarakis, Stylianos E.; Shimizu, Nobuyoshi; Krohn, Kai
IT CD34 (antigen)
CD40 (antigen)
CD80 (antigen)
CD86 (antigen)
Keratins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(autoimmune regulator gene AIRE is expressed in human cells regulating immune tolerance expressing)

L5 ANSWER 5 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:167516 BIOSIS
DOCUMENT NUMBER: PREV199900167516
TITLE: The role of accessory molecules in regulating cytokine production.
AUTHOR(S): Ozaki, M. E. (1); Luksch, C. R.; Winqvist, O.; **Karlsson, L.**; **Peterson, P. A.**; **Webb, S. R.**
CORPORATE SOURCE: (1) Scripps Res. Inst., La Jolla, CA 92037 USA
SOURCE: FASEB Journal, (March 12, 1999) Vol. 13, No. 4 PART 1, pp. A628.
Meeting Info.: Annual Meeting of the Professional Research Scientists for Experimental Biology 99 Washington, D.C., USA April 17-21, 1999
ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English
AU Ozaki, M. E. (1); Luksch, C. R.; Winqvist, O.; **Karlsson, L.**; **Peterson, P. A.**; **Webb, S. R.**
IT Major Concepts
Endocrine System (Chemical Coordination and Homeostasis)
IT Parts, Structures, & Systems of Organisms
antigen-presenting cells: immune system; **CD4** positive T cells: immune system; T cells: blood and lymphatics, immune system
IT Chemicals & Biochemicals
accessory molecules; **B7.1** molecule; B7.2 molecule; ICAM-1 [intercellular adhesion molecule-1]: expression; IL-10 [interleukin-10]: production; IL-4 [interleukin-4]: production

L5 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:1388 CAPLUS
DOCUMENT NUMBER: 128:60716
TITLE: MHC class II antigen presentation systems for **CD4+** T-cell activation, differentiation, and adoptive immunotherapy
INVENTOR(S): **Webb, Susan R.**; Winqvist, Ola; **Karlsson, Lars**; **Jackson, Michael R.**; **Peterson, Per A.**
PATENT ASSIGNEE(S): Scripps Research Institute, USA; Webb, Susan R.; Winqvist, Ola; Karlsson, Lars; Jackson, Michael R.; Peterson, Per A.
SOURCE: PCT Int. Appl., 141 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9746256	A1	19971211	WO 1997-US8697	19970522
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9732103	A1	19980105	AU 1997-32103	19970522
AU 723355	B2	20000824		
EP 969865	A1	20000112	EP 1997-927709	19970522
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2000511898	T2	20000912	JP 1998-500616	19970522
US 6355479	B1	20020312	US 1999-194285	19990412
PRIORITY APPLN. INFO.:			US 1996-18175P P	19960523
			WO 1997-US8697 W	19970522

AB The authors describe a method based on co-expression of selected MHC class II haplotypes in conjunction with one or more accessory mols. (e.g., **B7-1**) to activate **CD4+** T-cells and effect their differentiation to Th1 or Th2 subsets. Co-expression may be performed on solid supports, liposomes, and derivatized or transgenic cell lines. T-cells so activated cells may be suitable for adoptive immunotherapy.

TI MHC class II antigen presentation systems for **CD4+** T-cell activation, differentiation, and adoptive immunotherapy

IN **Webb, Susan R.**; Winqvist, Ola; **Karlsson, Lars**; **Jackson, Michael R.**; **Peterson, Per A.**

AB The authors describe a method based on co-expression of selected MHC class II haplotypes in conjunction with one or more accessory mols. (e.g., **B7-1**) to activate **CD4+** T-cells and effect their differentiation to Th1 or Th2 subsets. Co-expression may be performed on solid supports, liposomes, and derivatized or transgenic cell lines. T-cells so activated cells may be suitable for adoptive immunotherapy.

IT Drosophila
Spodoptera
(**CD4+** T-cell activation and differentiation via MHC class II antigen presentation system expressed in cells of)

IT CD antigens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CD70; of MHC class II antigen presentation systems for **CD4+** T-cell activation, differentiation, and adoptive immunotherapy)

IT Intestine, disease
(Crohn's; MHC class II antigen presentation systems for **CD4+** T-cell activation, differentiation, and adoptive immunotherapy of)

IT Histocompatibility antigens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(H-2, class II; MHC class II antigen presentation systems for **CD4+** T-cell activation, differentiation, and adoptive immunotherapy)

IT Histocompatibility antigens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(H-2M; of MHC class II antigen presentation systems for **CD4+** T-cell activation, differentiation, and adoptive immunotherapy)

IT Histocompatibility antigens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HLA, class II; antigen presentation systems for **CD4+** T-cell activation, differentiation, and adoptive immunotherapy)

IT Histocompatibility antigens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HLA-DM; of MHC class II antigen presentation systems for **CD4** + T-cell activation, differentiation, and adoptive immunotherapy)

IT Cell adhesion molecules
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ICAM-1 (intercellular adhesion mol. 1); of MHC class II antigen presentation systems for **CD4+** T-cell activation, differentiation, and adoptive immunotherapy)

IT Cell adhesion molecules
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ICAM-2 (intercellular adhesion mol. 2); of MHC class II antigen presentation systems for **CD4+** T-cell activation, differentiation, and adoptive immunotherapy)

IT Cell adhesion molecules
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ICAM-3 (intercellular adhesion mol. 3); of MHC class II antigen presentation systems for **CD4+** T-cell activation, differentiation, and adoptive immunotherapy)

IT Histocompatibility antigens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MHC (major histocompatibility complex), class II, biotinylated; of antigen presentation systems for **CD4+** T-cell activation, differentiation, and adoptive immunotherapy)

IT Adoptive immunotherapy
Animal tissue culture
Antigen presentation
Antigen processing
CD4-positive T cell
Cell differentiation
Immunological accessory cell
Membrane, biological
Temperature effects, biological
(MHC class II antigen presentation systems for **CD4+** T-cell activation, differentiation, and adoptive immunotherapy)

IT Cell adhesion molecules
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MHC class II antigen presentation systems for **CD4+** T-cell activation, differentiation, and adoptive immunotherapy)

IT Peptides, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(MHC class II antigen presentation systems for **CD4+** T-cell activation, differentiation, and adoptive immunotherapy)

IT Primers (nucleic acid)
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(MHC class II antigen presentation systems for **CD4+** T-cell activation, differentiation, and adoptive immunotherapy)

IT Allergy
Asthma
Autoimmune disease
Multiple sclerosis
Myasthenia gravis
(MHC class II antigen presentation systems for **CD4+** T-cell activation, differentiation, and adoptive immunotherapy of)

IT Animal cell line
(Schneider-2; of MHC class II antigen presentation systems for

CD4+ T-cell activation, differentiation, and adoptive immunotherapy)

IT Cell activation
(T cell; MHC class II antigen presentation systems for CD4+ T-cell activation, differentiation, and adoptive immunotherapy)

IT T cell (lymphocyte)
(activation; MHC class II antigen presentation systems for CD4+ T-cell activation, differentiation, and adoptive immunotherapy)

IT Porous materials
Porous materials
(adsorbents; for MHC class II antigen presentation systems for CD4+ T-cell activation, differentiation, and adoptive immunotherapy)

IT Synthetic gene
Synthetic gene
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(animal; of MHC class II antigen presentation systems for CD4+ T-cell activation, differentiation, and adoptive immunotherapy)

IT Thyroid gland, disease
(autoimmune thyroiditis; MHC class II antigen presentation systems for CD4+ T-cell activation, differentiation, and adoptive immunotherapy of)

IT Erythrocyte
(avidin-coated; of MHC class II antigen presentation systems for CD4+ T-cell activation, differentiation, and adoptive immunotherapy)

IT Phosphatidylethanolamines, biological studies
Phospholipids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates, with avidin; of MHC class II antigen presentation systems for CD4+ T-cell activation, differentiation, and adoptive immunotherapy)

IT Avidins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates, with phospholipids; of MHC class II antigen presentation systems for CD4+ T-cell activation, differentiation, and adoptive immunotherapy)

IT Dermatitis
(contact; MHC class II antigen presentation systems for CD4+ T-cell activation, differentiation, and adoptive immunotherapy of)

IT Virus vectors
(for MHC class II and co-stimulatory mol. expression for CD4+ T-cell activation in relation to adoptive immunotherapy)

IT Immobilization, biochemical
(for MHC class II antigen presentation systems for CD4+ T-cell activation, differentiation, and adoptive immunotherapy)

IT Epitopes
(for conjugation of MHC class II extracellular domains in antigen presentation systems for CD4+ T-cells)

IT Antibodies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(for crosslinking MHC class II extracellular domains in antigen presentation systems for CD4+ T-cells)

IT T cell (lymphocyte)
(helper cell/inducer, TH1; MHC class II antigen presentation systems for CD4+ T-cell activation, differentiation, and adoptive immunotherapy)

IT T cell (lymphocyte)
(helper cell/inducer, TH2; MHC class II antigen presentation systems for CD4+ T-cell activation, differentiation, and adoptive immunotherapy)

IT Intestine, disease
(inflammatory; MHC class II antigen presentation systems for CD4+ T-cell activation, differentiation, and adoptive immunotherapy of)

IT Diabetes mellitus
(insulin-dependent; MHC class II antigen presentation systems for CD4+ T-cell activation, differentiation, and adoptive immunotherapy of)

IT Gene, microbial
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(neoR; CD4+ T-cell activation and differentiation via MHC class II antigen presentation system in conjunction with)

IT Liposomes
Microtiter plates
(of MHC class II antigen presentation systems for CD4+ T-cell activation, differentiation, and adoptive immunotherapy)

IT CD80 (antigen)
CD86 (antigen)
Fas ligand
Invariant chain (class II antigen)
LFA-3 (antigen)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(of MHC class II antigen presentation systems for CD4+ T-cell activation, differentiation, and adoptive immunotherapy)

IT Promoter (genetic element)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(of MHC class II antigen presentation systems for CD4+ T-cell activation, differentiation, and adoptive immunotherapy)

IT Plasmids
(pRmHa-2 and pRmHa-3; for MHC class II and co-stimulatory mol. expression for CD4+ T-cell activation in relation to adoptive immunotherapy)

IT Adsorbents
Adsorbents
(porous; for MHC class II antigen presentation systems for CD4+ T-cell activation, differentiation, and adoptive immunotherapy)

IT Gene, animal
Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(synthetic; of MHC class II antigen presentation systems for CD4+ T-cell activation, differentiation, and adoptive immunotherapy)

IT Lupus erythematosus
(systemic; MHC class II antigen presentation systems for CD4+ T-cell activation, differentiation, and adoptive immunotherapy of)

IT 58-85-5D, Biotin, MHC class II conjugates
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(of MHC class II antigen presentation systems for **CD4**+ T-cell activation, differentiation, and adoptive immunotherapy)

L5 ANSWER 7 OF 7 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 96343863 MEDLINE
DOCUMENT NUMBER: 96343863 PubMed ID: 8760806
TITLE: Differing roles for B7 and intercellular adhesion molecule-1 in negative selection of thymocytes.
COMMENT: Comment in: J Exp Med. 1996 Aug 1;184(2):305-9
AUTHOR: Kishimoto H; Cai Z; Brunmark A; **Jackson M R**; **Peterson P A**; Sprent J
CORPORATE SOURCE: Department of Immunology, Scripps Research Institute, La Jolla, California 92037, USA.
CONTRACT NUMBER: AI21487 (NIAID)
CA25803 (NCI)
CA38355 (NCI)
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1996 Aug 1) 184 (2) 531-7.
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 19961008
Last Updated on STN: 19961008
Entered Medline: 19960923

AB To ensure self tolerance, immature thymocytes with high binding affinity for self peptides linked to major histocompatibility complex (MHC) molecules are eliminated in situ via apoptosis (negative selection). The roles of two costimulatory molecules, **B7-1** and intercellular adhesion molecule-1 (ICAM-1), in negative selection was examined by studying apoptosis of T cell receptor transgenic **CD4**+8+ thymocytes cultured with specific peptides presented by MHC class I-transfected Drosophila cells. When coexpressed on these cells, **B7-1** and ICAM-1 act synergistically and cause strong class 1-restricted negative selection of thymocytes. When expressed separately, however, **B7-1** and ICAM-1 display opposite functions: negative selection is augmented by **B7-1**, but is inhibited by ICAM-1. It is notable that **B7-1** is expressed selectively in the thymic medulla, whereas ICAM-1 is expressed throughout the thymus. Because of this distribution, the differing functions of **B7-1** and ICAM-1 may dictate the sites of positive and negative selection. Thus, in the cortex, the presence of ICAM-1, but not **B7-1**, on the cortical epithelium may preclude or reduce negative selection and thereby promote positive selection. Conversely, the combined expression of **B7-1** and ICAM-1 may define the medulla as the principal site of negative selection.

AU Kishimoto H; Cai Z; Brunmark A; **Jackson M R**; **Peterson P A**; Sprent J

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CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
Antigen-Presenting Cells: IM, immunology
***Antigens, CD80: PH, physiology**
Apoptosis
Cell Adhesion
Drosophila melanogaster
*Intercellular Adhesion Molecule-1: PH, physiology
Mice
Mice, Transgenic
Molecular Sequence Data
Peptides: . . .

CN 0 (Antigens, **CD80**); 0 (Peptides); 0 (Receptors, Antigen, T-Cell, alpha-beta)

=> dis his

(FILE 'HOME' ENTERED AT 10:03:54 ON 10 JUL 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 10:04:06 ON 10 JUL 2002
L1 14884 S WEBB S?/AU OR WINGVIST O?/AU OR KARLSSON L?/AU OR JACKSON M?/
L2 198 S L1 AND CD4?
L3 185 S L2 NOT CD40
L4 14 S L2 AND (CD80 OR B7.1)
L5 7 DUP REM L4 (7 DUPLICATES REMOVED)

=> s l5 and (ICAM? or CD54 or CD50 or CD102)
L6 5 L5 AND (ICAM? OR CD54 OR CD50 OR CD102)

=> dis l6 1-5 ibib abs

L6 ANSWER 1 OF 5 MEDLINE
ACCESSION NUMBER: 2001296822 MEDLINE
DOCUMENT NUMBER: 21270387 PubMed ID: 11376339
TITLE: A key role for **ICAM**-1 in generating effector cells mediating inflammatory responses.
AUTHOR: Camacho S A; Heath W R; Carbone F R; Sarvetnick N; LeBon A; **Karlsson L**; **Peterson P A**; **Webb S R**

CORPORATE SOURCE: Department of Immunology, IMM4, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA.
CONTRACT NUMBER: AI39664 (NIAID)
CA25803 (NCI)
CA41993 (NCI)
SOURCE: Nat Immunol, (2001 Jun) 2 (6) 523-9.
Journal code: 100941354. ISSN: 1529-2908.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010625
Last Updated on STN: 20010625
Entered Medline: 20010621

AB We investigated how the accessory molecule interactions encountered during T cell priming influence T cell-mediated destruction of insulin-producing beta cells and lead to type 1 diabetes. T cell receptor (TCR)-transgenic **CD4**+ T cells were primed under controlled conditions in vitro before being adoptively transferred into transgenic recipients expressing membrane ovalbumin under the control of the rat insulin promoter (RIP-mOVA). During priming, antigen-presenting cell expression of **B7-1** without intracellular adhesion molecule 1 (**ICAM**-1) led to the generation of effector cells that migrated to the pancreata of RIP-mOVA recipients but did not cause diabetes. In contrast, when T cells were primed with APCs expressing both **B7-1** and **ICAM**-1, pronounced destruction of beta cells and a rapid onset of diabetes were observed. Pathogenicity was associated with T cell production of the macrophage-attracting chemokines CCL3 and CCL4. Thus, interactions of lymphocyte function-associated antigen 1 with **ICAM**-1 during priming induce both qualitative and quantitative alterations in T effector function and induce potentially autodestructive responses.

L6 ANSWER 2 OF 5 MEDLINE
ACCESSION NUMBER: 1999179008 MEDLINE
DOCUMENT NUMBER: 99179008 PubMed ID: 10077630
TITLE: Intercellular adhesion molecule-1 inhibits interleukin 4 production by naive T cells.
AUTHOR: Luksch C R; Winqvist O; Ozaki M E; **Karlsson L**; **Jackson M R**; **Peterson P A**; **Webb S R**
CORPORATE SOURCE: Department of Immunology, IMM4, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA.
CONTRACT NUMBER: CA25803 (NCI)
CA41993 (NCI)
+
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Mar 16) 96 (6) 3023-8.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990601
Last Updated on STN: 19990601
Entered Medline: 19990520

AB The type of cytokines produced during T cell responses determines susceptibility or resistance to many pathogens and influences the development of autoimmunity and allergy. To define the role of individual accessory molecules in cytokine production during primary immune responses, Drosophila cell lines expressing murine major histocompatibility complex class II molecules with defined combinations of accessory molecules were used to present peptide antigen to naive T cell receptor transgenic T cells. Significantly, expression of **B7-1** or B7.2 without additional accessory molecules led to very high production of interleukin (IL)-4, which contrasted with minimal IL-4 production elicited by conventional antigen presenting cells (APC). However, coexpression of **ICAM**-1 and B7 on Drosophila APC induced little IL-4, suggesting an inhibitory role for intercellular adhesion molecule-1 (**ICAM**-1). In support of this idea, stimulation of T cell receptor transgenic T cells with peptide presented by splenic APC devoid of **ICAM**-1 (from **ICAM**-1-deficient mice) led to high IL-4 production. Thus, the level of IL-4 production by naive **CD4**(+) T cells during typical primary responses appears to be controlled, at least in part, by T-APC interactions involving **ICAM**-1.

L6 ANSWER 3 OF 5 MEDLINE
ACCESSION NUMBER: 96343863 MEDLINE
DOCUMENT NUMBER: 96343863 PubMed ID: 8760806
TITLE: Differing roles for B7 and intercellular adhesion molecule-1 in negative selection of thymocytes.
COMMENT: Comment in: J Exp Med. 1996 Aug 1;184(2):305-9
AUTHOR: Kishimoto H; Cai Z; Brunmark A; **Jackson M R**; **Peterson P A**; Sprent J
CORPORATE SOURCE: Department of Immunology, Scripps Research Institute, La Jolla, California 92037, USA.
CONTRACT NUMBER: AI21487 (NIAID)
CA25803 (NCI)
CA38355 (NCI)
+
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1996 Aug 1) 184 (2) 531-7.
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 19961008
Last Updated on STN: 19961008
Entered Medline: 19960923

AB To ensure self tolerance, immature thymocytes with high binding affinity for self peptides linked to major histocompatibility complex (MHC) molecules are eliminated in situ via apoptosis (negative selection). The roles of two costimulatory molecules, **B7-1** and intercellular adhesion molecule-1 (**ICAM**-1), in negative selection was examined by studying apoptosis of T cell receptor transgenic **CD4**+8+ thymocytes cultured with specific peptides presented by MHC

class I-transfected Drosophila cells. When coexpressed on these cells, **B7-1** and **ICAM**-1 act synergistically and cause strong class 1-restricted negative selection of thymocytes. When expressed separately, however, **B7-1** and **ICAM**-1 display opposite functions: negative selection is augmented by **B7-1**, but is inhibited by **ICAM**-1. It is notable that **B7-1** is expressed selectively in the thymic medulla, whereas **ICAM**-1 is expressed throughout the thymus. Because of this distribution, the differing functions of **B7**-1 and **ICAM**-1 may dictate the sites of positive and negative selection. Thus, in the cortex, the presence of **ICAM**-1, but not **B7-1**, on the cortical epithelium may preclude or reduce negative selection and thereby promote positive selection. Conversely, the combined expression of **B7**-1 and **ICAM**-1 may define the medulla as the principal site of negative selection.

L6 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:1388 CAPLUS
DOCUMENT NUMBER: 128:60716
TITLE: MHC class II antigen presentation systems for **CD4+** T-cell activation, differentiation, and adoptive immunotherapy
INVENTOR(S): **Webb, Susan R.**; Winqvist, Ola; **Karlsson, Lars**; **Jackson, Michael R.**; **Peterson, Per A.**
PATENT ASSIGNEE(S): Scripps Research Institute, USA; Webb, Susan R.; Winqvist, Ola; Karlsson, Lars; Jackson, Michael R.; Peterson, Per A.
SOURCE: PCT Int. Appl., 141 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9746256	A1	19971211	WO 1997-US8697	19970522
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9732103	A1	19980105	AU 1997-32103	19970522
AU 723355	B2	20000824		
EP 969865	A1	20000112	EP 1997-927709	19970522
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2000511898	T2	20000912	JP 1998-500616	19970522
US 6355479	B1	20020312	US 1999-194285	19990412

PRIORITY APPLN. INFO.: US 1996-18175P P 19960523
WO 1997-US8697 W 19970522

AB The authors describe a method based on co-expression of selected MHC class II haplotypes in conjunction with one or more accessory mols. (e.g., **B7-1**) to activate **CD4+** T-cells and effect their differentiation to Th1 or Th2 subsets. Co-expression may be performed on solid supports, liposomes, and derivatized or transgenic cell lines. T-cells so activated cells may be suitable for adoptive immunotherapy.

L6 ANSWER 5 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:167516 BIOSIS
DOCUMENT NUMBER: PREV199900167516
TITLE: The role of accessory molecules in regulating cytokine production.
AUTHOR(S): Ozaki, M. E. (1); Luksch, C. R.; Winqvist, O.; **Karlsson, L.**; **Peterson, P. A.**; **Webb, S. R.**
CORPORATE SOURCE: (1) Scripps Res. Inst., La Jolla, CA 92037 USA
SOURCE: FASEB Journal, (March 12, 1999) Vol. 13, No. 4 PART 1, pp. A628.
Meeting Info.: Annual Meeting of the Professional Research Scientists for Experimental Biology 99 Washington, D.C., USA April 17-21, 1999
ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English

=> dis his

(FILE 'HOME' ENTERED AT 10:03:54 ON 10 JUL 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 10:04:06 ON 10 JUL 2002
L1 14884 S WEBB S?/AU OR WINGVIST O?/AU OR KARLSSON L?/AU OR JACKSON M?/
L2 198 S L1 AND CD4?
L3 185 S L2 NOT CD40
L4 14 S L2 AND (CD80 OR B7.1)
L5 7 DUP REM L4 (7 DUPLICATES REMOVED)
L6 5 S L5 AND (ICAM? OR CD54 OR CD50 OR CD102)

=> s cd4?
L7 233993 CD4?

=> s l7 not cd40
L8 217789 L7 NOT CD40

=> s l8 and (CD80 or B7.1)
L9 2210 L8 AND (CD80 OR B7.1)

=> s l9 and (ICAM? OR CD54 OR CD50 OR CD102)
L10 322 L9 AND (ICAM? OR CD54 OR CD50 OR CD102)

=> s l10 and PD<1996-523
NUMERIC VALUE NOT VALID '1996-523'
DATE SPECIFICATION IS NOT VALID
DATE SPECIFICATION IS NOT VALID
DATE SPECIFICATION IS NOT VALID
Date specifications may use ranges and numeric operators. The date itself can be in any of the following general formats:

STN Format: YYYYMMDD

Slash Format: MM/DD/YYYY or MM/YYYY

Dot Format: DD.MM.YYYY or MM.YYYY

Text Format:		
	February 10, 1987	Feb 1989
	Feb. 10, 1987	1990
	Feb. 10, 2000	1998 - 2001
	Feb 10, 1987	July 1997 - May 2002
	10 February 1987	March 5 - 8, 1990
	10 Feb 2007	April - June, 1999

Any year entered with only two digits will be interpreted as being in the range 1900-1999. Thus, Mar 12 01 will be searched as 19010312.

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PROCESSING COMPLETED FOR L11
L12          34 DUP REM L11 (38 DUPLICATES REMOVED)

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L12  ANSWER 1 OF 34  CAPLUS  COPYRIGHT 2002 ACS        DUPLICATE 1
ACCESSION NUMBER:        1996:282494  CAPLUS
DOCUMENT NUMBER:         124:314846
TITLE:                   Intercellular adhesion molecule-1 is necessary but not
                         sufficient to activate CD4+ T cells.
                         Discovery of a novel costimulator on kidney tubule
                         cells
AUTHOR(S):               Hagerty, David T.
CORPORATE SOURCE:        Dep. Med. Pathol., Washington Univ. Sch. Med., St.
                         Louis, MO, 63110, USA
SOURCE:                  J. Immunol. (1996), 156(10), 3652-3659
                         CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   Kidney tubule cells (KTC) are targets of T lymphocyte injury during
     allograft rejection and interstitial nephritis.  KTC process and present
     self- and foreign Ags for immune recognition by CD4+ T cells in
     vivo and in vitro.  However, it is not known whether KTC can provide the
     costimulatory signal required to fully activate CD4+ T cells.
     Using the MRL/MpJ fas .ltbbrac.lpr.rtbbrac. model of lupus interstitial
     nephritis, we found that KTC did not express the costimulators B7
     -1 or B7-2.  Nevertheless, KTC from both normal and systemically
     infected mice provided non-B7 costimulation to splenic CD4+ T
     cells.  T cell proliferation was blocked by mAbs binding intercellular
     adhesion mol.-1 (ICAM-1) but not by mAb or fusion proteins
     binding B7-1, B7-2, heat-stable Ag, or vascular cell
     adhesion mol.-1.  Importantly, ICAM-1 expression was necessary
     but not sufficient to provide costimulation.  The transformed KTC line
     D3.B7- expressed high levels of ICAM-1 but did not provide
     costimulation.  Interestingly, KTC provided costimulation to splenic T
     cells but not to a Th1 clone.  These results show that freshly isolated
     KTC can provide non-B7 costimulation to splenic T cells via an
     unidentified costimulator and ICAM-1.  Furthermore, these expts.
     demonstrate the complex nature of T cell activation and show that at least
     for splenic T cells, three or more signals may be required for full
     activation on live APC.

L12  ANSWER 2 OF 34  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:        1996:632279  CAPLUS
DOCUMENT NUMBER:         125:273089
TITLE:                   Naive and effector CD4 T cells differ in
                         their requirements for T cell receptor versus
                         costimulatory signals
AUTHOR(S):               Dubey, Caroline; Croft, Michael; Swain, Susan L.
CORPORATE SOURCE:        Hospital Broussais, INSERM Unit 430, Paris, Fr.
SOURCE:                  J. Immunol. (1996), 157(8), 3280-3289
                         CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   The authors used naive CD4 cells and in vitro-derived Th1 and
     Th2 effectors from TCR transgenic mice to investigate the requirements of
     the subsets for TCR signaling and interactions with accessory mols.
     Peptide antigens (Ag) and immobilized anti-CD3 were used to provide
     different TCR signals.  Anti-CD28 Ab or a panel of class II+ fibroblasts,
     expressing no accessory mols. or expressing intracellular adhesion mol.-1,
     B7-1, or both mols., were used as APC or accessory cells
     (AC).  An efficient naive T cell response required a strong TCR signal
     (high dose anti-CD3 or peptide) and high levels of multiple synergizing
     costimulatory signals, while effector cells responded efficiently to
     anti-CD3 alone.  Addn. of AC only slightly augmented the effector
     responses.  Effectors responded to lower doses of peptide than naive
     cells.  However, when peptide-pulsed APC were used to stimulate effectors,
     requirements varied with the cytokine measured.  The prodn. of IL-4 did
     not require accessory mols. on APC.  IL-2 prodn. required interacting APC
     to express accessory mols., but was little augmented by AC not presenting
     Ag, suggesting a requirement for noncostimulatory interactions.
     Proliferation of effectors closely paralleled IL-2 prodn.  Prodn. of
     IFN-.gamma. was intermediate in dependence on accessory mols., and prodn.
     of IL-5 was nearly as dependent as IL-2.  These results establish major
     differences between the induction of naive and effector responses and
     document differential requirements for the induction of distinct
     cytokines, indicating that different cytokines may be produced depending
     on the context of effector restimulation.

L12  ANSWER 3 OF 34  CAPLUS  COPYRIGHT 2002 ACS        DUPLICATE 2
ACCESSION NUMBER:        1996:565015  CAPLUS
DOCUMENT NUMBER:         125:219233
TITLE:                   Rapid induction of tumor necrosis factor cytotoxicity
                         in naive splenic T cells by simultaneous CD80
                         (B7.1) and CD54 (
                         ICAM-1) co-stimulation
AUTHOR(S):               Nishio, Makoto; Podack, Eckhard R.
CORPORATE SOURCE:        Dep. Microbiology Immunology, Univ. Miami School
                         Medicine, Miami, FL, USA
```

SOURCE: Eur. J. Immunol. (1996), 26(9), 2160-2164
CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The co-expression of B7.1 (CD80) and intercellular adhesion mol. (ICAM)-1 (CD54) on tumor cells can induce tumor immunity and immunol. memory. We show here that the non-immunogenic tumor lines Lewis lung carcinoma and B16F10 melanoma, co-transfected with B7.1 and ICAM-1, induced cytotoxic levels of membrane tumor necrosis factor (TNF) on naive syngeneic T cells within 24 h. Membrane TNF expression, primarily on CD4 cells, was responsible for tumor cell lysis by naive spleen cells and could be completely abolished by anti-TNF antiserum. It is suggested that the strong induction of TNF cytotoxicity may be important in the establishment of tumor immunity.

L12 ANSWER 4 OF 34 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:491349 CAPLUS
DOCUMENT NUMBER: 125:165520
TITLE: T-T cellular interaction between CD4-CD8- regulatory T cells and T cell clones presenting TCR peptide. Its implications for TCR vaccination against experimental autoimmune encephalomyelitis
AUTHOR(S): Kozovska, Milena F.; Yamamura, Takashi; Tabira, Takeshi
CORPORATE SOURCE: Dep. Demyelinating Dis. Aging, Natl. Cent. Neurol. Psychiatry, Kodaira, Japan
SOURCE: J. Immunol. (1996), 157(4), 1781-1790
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Regulatory T cells recognizing TCR determinants presumably play a crit. role in the control of exptl. autoimmune encephalomyelitis, a prototype tissue-specific autoimmune disease. This study was initiated to det. whether regulatory T cells can be induced against a V.beta.17a CDR2 peptide (residues 50-68) in SJL/J mice. Although the TCR peptide showed regulatory effects in vivo, the presence of T cells specific for the peptide could not be proven with conventional proliferation assays. Unexpectedly, in the presence of myelin basic protein-specific T clone cells (Tcc), the sensitized spleen cells vigorously proliferated in response to the TCR peptide. The subsequent expt. showed that this was due to the outstanding capability of the Tcc as APC for the exogenous TCR peptide. Using the Tcc as APC, the authors were able to establish V.beta.17a50-68-specific T cell lines from in vivo primed spleen cells. The line cells were MHC class I restricted and dominated by T cells with a distinct surface phenotype (CD4-CD8-V.beta.17a+). Presentation of the peptide by the Tcc was inhibited by treatment with gelonin that could block a MHC class I presentation pathway. The ability of T cells to present the TCR peptide was not related to their Ag specificity, but correlated with the expression levels of MHC class I mols. and adhesion mols. such as intercellular adhesion mol.-1 and B7-1 on their surface. The TCR peptide-specific T cells produced a sol. mediator(s) that is inhibitory for T cell activation and were protective against actively induced exptl. autoimmune encephalomyelitis. These results show that V.beta.17a50-68 vaccination induces regulatory CD4-CD8- T cells that could interact with T cells presenting relevant TCR fragments.

L12 ANSWER 5 OF 34 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:98208 CAPLUS
DOCUMENT NUMBER: 124:143273
TITLE: In vivo blockade of TNF-.alpha. by intravenous infusion of a chimeric monoclonal TNF-.alpha. antibody in patients with rheumatoid arthritis. Short term cellular and molecular effects
AUTHOR(S): Lorenz, Hanns-Martin; Antoni, Christian; Valerius, Thomas; Repp, Roland; Gruenke, Mathias; Schwerdtner, Nives; Nuesslein, Hubert; Woody, Jim; Kalden, Joachim R.; et al.
CORPORATE SOURCE: Dep. Internal Medicine, Univ. Erlangen-Nuremberg, Erlangen, Germany
SOURCE: J. Immunol. (1996), 156(4), 1646-53
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Due to the unknown etiol. of RA, specific treatment is not available. Recently, in a double-blinded, placebo-controlled clin. trial, in vivo blockade of TNF-.alpha. by a single infusion of a chimeric TNF-.alpha.-blocking mAb, cA2, has proven to be highly effective in the treatment of RA. In parallel to this trial, the authors tested the consequences of cA2 infusion in ex vivo and in vitro expts. In this paper, the authors describe an increase in CD4+ and CD8+ T lymphocyte counts on day 1 and a marked decrease in monocyte counts preferentially on day 7 after cA2 treatment, without major changes in B lymphocyte or NK cell counts. In addn., the authors found an increased responsiveness of PBMC to CD28 mAb/PMA, but not to CD3 mAb, superantigen staphylococcus enterotoxin B, or PHA on day 1 after infusion. The increase in DNA synthesis of PBMC was paralleled by increased IL-2 mRNA and IL-4 mRNA expression and IL-2 protein secretion in culture supernatants after in vitro stimulation of PBMC with CD28 mAb/PMA. In PBMC, the authors did not find any significant changes in mRNA or protein expression of CD28 Ag or CD28 ligands, B7-1 and B7-2. Serum concns. of IL-1.beta., IL-6, and sol. CD14 were significantly diminished after in vivo TNF-.alpha. blockade. The authors did not see relevant changes in granulocyte function in vitro after cA2 infusion. Finally, the authors obsd. a statistically significant decrease in sICAM-1 mols. in the serum of patients treated with serum compared with that in the serum of subjects given placebo. This change in sICAM-1 concn. was evident on days 1 and 7 after the infusion of 10 mg/kg cA2, whereas it occurred only on day 7 in the serum of patients treated with the low dose (1 mg/kg) of cA2.

L12 ANSWER 6 OF 34 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:305664 CAPLUS
DOCUMENT NUMBER: 125:7787
TITLE: Specific acceptance of cardiac allografts after treatment with antibodies to CD80 and CD86 in mice
AUTHOR(S): Bashuda, H.; Seino, K.; Kano, M.; Sato, K.; Azuma, M.; Yagita, H.; Okumura, K.
CORPORATE SOURCE: School Medicine, Juntendo University, Tokyo, 113, Japan
SOURCE: Transplant. Proc. (1996), 28(2), 1039-1041

CODEN: TRPPA8; ISSN: 0041-1345
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Recent studies have demonstrated that administration of monoclonal antibodies to some intercellular adhesion mols., such as LFA-1/ **ICAM**-1, CD2/**CD48**, or VLA-4/VCAM-1, led to an indefinite allograft survival. In this study, the authors show that treatment with anti-**CD80**/CD86 MAbs could induce allospecific tolerance in a murine cardiac transplantation model.

L12 ANSWER 7 OF 34 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
ACCESSION NUMBER: 1996:340157 CAPLUS
DOCUMENT NUMBER: 125:31679
TITLE: Development and characterization of a novel monoclonal antibody (mNI-11) that induces cell adhesion of the LPS-stimulated human monocyte-like cell line U937
AUTHOR(S): Ikewaki, Nobunao; Inoko, Hidetoshi
CORPORATE SOURCE: Dep. of Micribiology, Tokai University School of Medicine, Isehara, Japan
SOURCE: J. Leukocyte Biol. (**1996**), 59(5), 697-708
CODEN: JLBIE7; ISSN: 0741-5400
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A monoclonal IgG1 antibody (mAb), designated mNI-11, was produced by immunizing mice with the lipopolysaccharide (LPS)-stimulated monocyte-like cell line U937. The reactivity of mNI-11 was tested by the indirect immunofluorescence method. The antigen defined by mNI-11 was expressed on U937 cells, LPS-stimulated U937 cells, normal CD14+ cells (monocytes/macrophages), and human umbilical vein endothelial cells (HUVECs). Expression of the antigen defined by mNI-11 on HUVECs slightly increased in response to exposure to tumor necrosis factor-.alpha. (TNF-.alpha.) and phorbol myristate acetate (PMA). When the reactivity of mNI-11 and mAbs binding human differentiation antigens such as CD11a, CD11b, CD11c, CD14, CD16, CD18, CD23, CD28, CD29, CD31, **CD43**, **CD44**, **CD45RA**, **CD49d**, **CD50**, **CD54**, CD58, **CD80**, **CD102**, CD106, HLA-class I, or HLA-class II antigen was compared, no mNI-11 reactivity resembling that of these mAbs was found. MNI-11 markedly induced homotypic cell aggregation of U937 cells when they were stimulated with LPS. The mNI-11-induced aggregation of LPS-stimulated U937 cells, referred to as LPS-U937 cells, required neither Fc receptor engagement nor crosslinking of the antigen defined by mNI-11 because aggregation was induced by both F(ab')2 fragments and monovalent F(ab') fragments of MNI-11. The mNI-11-induced aggregation was blocked by the addn. of EDTA, and also when incubated at 4.degree.. MAbs to CD11a/CD18 (lymphocyte-function assocd. antigen-1; LFA-1) and **CD54** (intercellular adhesion mol.-1; **ICAM**-1) completely blocked the LPS-U937 cell aggregation induced by mNI-11. The LPS-U937 cell aggregation induced by mNI-11 was partially but not completely blocked by the protein kinase C inhibitors sphingosine and H-7, and was completely blocked by the protein-tyrosine kinase inhibitor genistein. Interestingly, mNI-11 markedly promoted LPS-U937 cell adhesion to HUVECs. The mNI-11 induced LPS-U937 cell adhesion to HUVECs was not reduced in the presence of LFA-1 (CD11a/CD18) or **ICAM**-1 (**CD54**) mAbs. LPS-U937 cells, whether treated with mNI-11 or not, sufficiently adhered to the extracellular matrix protein fibronectin, but not to laminin or collagen type I. However, mNI-11 did not markedly promote LPS-U937 cell adhesion to fibronectin. Adhesion of LPS-U937 cells treated with mNI-11 to fibronectin was completely blocked by CD29 (.beta. chain of very late antigens) mAb. The surface antigen recognized by mNI-11 had a mol. size of .apprx.97 kDa under non-reducing conditions and .apprx.117 kDa under reducing conditions, as detd. by immunoblotting anal. The authors found that mNI-11 recognizes an adhesion-assocd. mol. distinct from any previously reported in terms of its pattern of cellular distribution and mol. wt., and also found that mNI-11 has activity which induces cell adhesion/aggregation of U937 cells when stimulated with LPS.

L12 ANSWER 8 OF 34 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 4
ACCESSION NUMBER: 1996:584820 CAPLUS
DOCUMENT NUMBER: 125:245461
TITLE: Immunogenicity of biliary epithelium: Investigation of antigen presentation to **CD4**+T cells
AUTHOR(S): Leon, Maria P.; Bassendine, Margaret F.; Wilson, Julia L.; Ali, Simi; Thick, Michael; Kirby, John A.
CORPORATE SOURCE: Medical School, University Newcastle upon Tyne, Newcastle upon Tyne, NE2 4HH, UK
SOURCE: Hepatology (Philadelphia) (**1996**), 24(3), 561-567
CODEN: HPTLD9; ISSN: 0270-9139
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The intrahepatic biliary epithelium is susceptible to extensive T-cell-mediated damage during primary biliary cirrhosis, primary sclerosing cholangitis, and hepatic allograft rejection. During these processes, human intrahepatic biliary epithelial cells (HIBEC) become activated and express high levels of the lymphocyte adhesion mols., intercellular adhesion mol.-1 (**ICAM**-1) and lymphocyte-assocd. antigen (LFA)-3, and of class II MHC antigens. It follows that activated HIBEC may also play a direct role in the activation of antigen-specific **CD4**+ T lymphocytes. The capacity of class II MHC antigen-expressing HIBEC to present antigen and induce specific proliferation of **CD4**+ T cells was examd. in this study. Lines of purified HIBEC were activated by culture with the proinflammatory cytokines interferon gamma (IFN-.gamma.) and tumor necrosis factor .alpha. and were mixed in coculture with allogeneic **CD4**+ T cells. The result of interaction between these cells was assessed by measurement of lymphoproliferation and IL-2 prodn. Class II MHC antigen-expressing HIBEC failed to induce either lymphoproliferation or IL-2 prodn. However, both of these parameters of T-cell activation were pos. in cocultures when a costimulation signal was delivered to T cells by adding bivalent anti-CD28 antibodies. The antigen-specific activation of these T cells was further enhanced by the addn. of a crosslinking secondary antibody that caused CD28 receptor aggregation. The failure of cytokine-stimulated HIBEC to induce T-cell activation is consistent with the observation that HIBEC do not express the costimulatory CD28 ligands **B7-1** or B7-2 at either mRNA or protein levels. It may be concluded that HIBEC are unlikely to play a direct role in activation of antigen-specific **CD4**+ T lymphocytes within the inflamed liver.

L12 ANSWER 9 OF 34 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 5
ACCESSION NUMBER: 1996:504816 CAPLUS
DOCUMENT NUMBER: 125:165648
TITLE: Differing roles for B7 and intercellular adhesion

molecule-1 in negative selection of thymocytes
AUTHOR(S): Kishimoto, Hidehiro; Cai, Zeling; Brunmark, Anders; Jackson, Michael R.; Peterson, Per A.; Sprent, Jonathan
CORPORATE SOURCE: Dep. Immunol., Scripps Res. Inst., La Jolla, CA, 92037., USA
SOURCE: J. Exp. Med. (1996), 184(2), 531-537
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To ensure self tolerance, immature thymocytes with high binding affinity for self peptides linked to major histocompatibility complex (MHC) mols. are eliminated in situ via apoptosis (neg. selection). The roles of two costimulatory mols., **B7-1** and intercellular adhesion mol.-1 (**ICAM**-1), in neg. selection was examd. by studying apoptosis of T cell receptor transgenic **CD4**+8+ thymocytes cultured with specific peptides presented by MHC class I-transfected Drosophila cells. When coexpressed on these cells, **B7-1** and **ICAM**-1 act synergistically and cause strong class I-restricted neg. selection of thymocytes. When expressed sep., however, **B7-1** and **ICAM**-1 display opposite functions: neg. selection is augmented by **B7-1**, but is inhibited by **ICAM**-1. It is notable that **B7-1** is expressed selectively in the thymic medulla, whereas **ICAM**-1 is expressed throughout the thymus. Because of this distribution, the differing functions of **B7-1** and **ICAM**-1 may dictate the sites of pos. and neg. selection. Thus, in the cortex, the presence of **ICAM**-1, but not **B7-1**, on the cortical epithelium may preclude or reduce neg. selection and thereby promote pos. selection. Conversely, the combined expression of **B7-1** and **ICAM**-1 may define the medulla as the principal site of neg. selection.

L12 ANSWER 10 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:159793 BIOSIS
DOCUMENT NUMBER: PREV199799458996
TITLE: MHC class II-mediated antigen presentation by melanoma cells.
AUTHOR(S): Brady, Mary S. (1); Eckels, David D.; Ree, Sophia Y.; Schultheiss, Kim E.; Lee, Janet S.
CORPORATE SOURCE: (1) Memorial Sloan-Kettering Cancer Cent., 1275 York Avenue, New York, NY 10021 USA
SOURCE: Journal of Immunotherapy with Emphasis on Tumor Immunology, (1996) Vol. 19, No. 6, pp. 387-397.
ISSN: 1067-5582.
DOCUMENT TYPE: Article
LANGUAGE: English

AB Constitutive expression of major histocompatibility complex (MHC) class II molecules is normally restricted to professional antigen-presenting cells (APCs) of the immune system, although it also occurs frequently in melanoma. Clinical evidence suggesting that MHC class II expression by melanoma is associated with tumor progression led us to postulate a role for MHC class II-mediated antigen presentation in this disease. First, we investigated whether melanoma cells derived from metastases can process antigen and/or present peptide vi MHC class II molecules to a peptide-specific **CD4**+ T-cell clone. In all cell lines tested, melanoma cells were able to process antigen and present peptide efficiently to **CD4**+ T cells, resulting in T-cell proliferation increased 5-26-fold over controls. Next, we found that CD28-mediated costimulation was not required, because blocking with CTLA4Ig had no effect on the T-cell response to either melanoma or B cells as APCs. In contrast, blocking **CD54** (**ICAM**-1) resulted in a decrease in proliferation in response to peptide presentation by melanoma but not B cells. These data demonstrate that MHC class II molecules on melanoma cells are functional and that antigen-processing pathways are intact. In addition, **CD54** seems to play a significant role in peptide presentation by melanoma.

L12 ANSWER 11 OF 34 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 6
ACCESSION NUMBER: 1996:125795 CAPLUS
DOCUMENT NUMBER: 124:173266
TITLE: Cultured human Langerhans' cells are superior to fresh cells at presenting native HIV-1 protein antigens to specific **CD4**+ T-cell lines
AUTHOR(S): Girolomoni, G.; Valle, M. T.; Zacchi, V.; Costa, M. G.; Giannetti, A.; Manca, F.
CORPORATE SOURCE: Istituto Dermopatico dell'Immunacolata, IRCCS, Rome, Italy
SOURCE: Immunology (1996), 87(2), 310-16
CODEN: IMMUAM; ISSN: 0019-2805
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cultured Langerhans' cells (CLC) exhibit enhanced antigen-presenting function compared to freshly isolated LC (FLC), but they are commonly believed to be inefficient at processing intact proteins. In this study, FLC and CLC from normal, human immunodeficiency virus (HIV) seroneg. volunteers were compared for their ability to present the HIV-1 envelope glycoprotein gp120 or reverse transcriptase (p66) antigens to autologous, specific **CD4**+ T cell lines. Epidermal cell suspensions enriched for LC were prepd. from suction blister roofs. FLC stimulated T cells at lower antigen concns. compared to unfractionated peripheral blood mononuclear cells (PBMC). CLC were more potent on a per cell basis than FLC, PBMC or adherent monocytes at presenting native gp120, native p66 or immunogenic peptides. CLC were also more efficient than FLC or PBMC in terms of the amt. of antigen required for T-cell activation. Chloroquine and leupeptin inhibited presentation of intact p66, but not of an immunodominant peptide, by FLC or CLC, thus indicating that both cells utilize antigen processing mechanisms that are based on intracellular acidification and protease activity. Incubation of CLC with monoclonal antibodies against HLA-DR, CD11b, CD18, **CD50**, **CD54**, CD58 or **CD80**, but not anti-major histocompatibility complex class I (MHC-I), inhibited antigen-specific T-cell proliferation to varying degrees. We conclude that human CLC retain the ability to process and present protein antigens potently to **CD4**+ T cells. Thus, CLC have the capacity to participate actively in the generation and maintenance of T-helper cell immunity to viral antigens during HIV-1 infection.

L12 ANSWER 12 OF 34 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 7
ACCESSION NUMBER: 1996:450503 CAPLUS
DOCUMENT NUMBER: 125:140301
TITLE: Antigen-presenting-cell function of interferon .gamma.-treated human gingival fibroblasts

AUTHOR(S): Shimabukuro, Yoshio; Murakami, Shinya; Okada, Hiroshi
CORPORATE SOURCE: Faculty Dentistry, Osaka University, Suita, 565, Japan
SOURCE: J. Periodontal Res. (1996), 31(3), 217-228
CODEN: JPDRAY; ISSN: 0022-3484
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present study was carried out to examine the antigen-presenting cell (APC) functions of human gingival fibroblasts (HGF) elicited with IFN.gamma.. Stimulation of HGF with IFN.gamma. clearly induced HLA-DR expression and enhanced expression of intercellular adhesion mol.-1 (**ICAM**-1) on HGF. Despite the phenotypical resemblance of IFN.gamma.-treated HGF to so-called APC, HLA-DR pos. HGF were unable to induce proliferation of allo-reactive peripheral blood T cells (PBT) isolated from different donors. The failure of IFN.gamma.-treated HGF to stimulate unprimed allo-reactive PBT was not due to the lack of prodn. of IL-1 or the immunosuppressive effect of PGE2 from HGF. The fact that detectable expression of **CD80**, ligand for CD28, was not found on IFN.gamma.-treated HGF may at least in part explain the ineffective function of HGF as APC. Interestingly, IFN.gamma.-treated HGF induced proliferation of primed allo-reactive **CD4**+ T cells in a HLA-DR dependent manner, suggesting that IFN.gamma.-treated HGF may have the ability to stimulate pre-activated T cells. We then confirmed that high levels of IFN.gamma. mRNA were detectable in inflamed gingival tissue. Although it cannot be concluded from this study that HGF are incapable of effectively presenting antigenic peptides to autologous T cells bearing appropriate T cell receptors, present results suggest that HGF may be affected by locally-secreted IFN.gamma. and that the IFN.gamma.-stimulated HGF may play a role in regulating immune responsiveness in inflammatory periodontal lesions.

L12 ANSWER 13 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97133287 EMBASE
DOCUMENT NUMBER: 1997133287
TITLE: Human thymic epithelial cells present superantigens to T-cell lines and thymocytes.
AUTHOR: Jorgensen A.; Nielsen M.; Svejgaard A.; Ledbetter J.A.; Odum N.; Ropke C.
CORPORATE SOURCE: C. Ropke, Institute of Medical Anatomy, University of Copenhagen, The Panum Institute, Blegdamsvej 3, DK-2200 Copenhagen N, Denmark. C.Ropke@mai.ku.dk
SOURCE: Experimental and Clinical Immunogenetics, (1996) 13/3-4 (192-203).
Refs: 40
ISSN: 0254-9670 CODEN: ECIME4
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB It is generally accepted that thymic epithelial cells (TEC) act as accessory cells in positive selection of pre-T cells. However, our knowledge of the antigen presentation and accessory cell function of human TEC is limited. Here we present results obtained by the use of serum-free cultured human TEC, showing that IFN-.gamma.-treated TEC are able to support T-cell-mediated responses to the bacterial superantigens (Sag) SEA and SEB, even at very low Sag concentrations. T-cell responses to TEC-presented Sags were dependent on the presence of the adhesion molecules **ICAM**-1, **ICAM**-2, LFA-1, and LFA-3, but not on **CD4** and CD8 molecules. There is a low but significant expression of B7 molecules on human TEC, and treatment of TEC with anti-**B7.1** and anti-B7.2 antibodies before Sag pulsing leads to decreased Sag responses, indicating a significant importance of B7 molecules on TEC. Both **CD4**+ T-cell lines and **CD4**+ as well as CD8+ subpopulations of thymocytes showed significant responses, whereas nonseparated thymocytes, **CD4**+8+, and **CD4**-CD8- thymocytes did not respond or showed very low responses. In conclusion, the present results demonstrate that cultured human TEC are able to present Sag to thymocytes.

L12 ANSWER 14 OF 34 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 8
ACCESSION NUMBER: 1996:650575 CAPLUS
DOCUMENT NUMBER: 125:325816
TITLE: A novel monoclonal antibody mNI-58A against the .alpha.-chain of leukocyte function-associated antigen-1 (LFA-1) blocks the homotypic cell aggregation and actively regulates morphological changes in the phorbol myristate acetate (PMA)-activated human monocyte-like cell line, U937
AUTHOR(S): Ikewaki, N.; Yamada, A.; Sonoda, A.; Inoko, H.
CORPORATE SOURCE: School Nursing, Kitasato University, Kanagawa, Japan
SOURCE: Tissue Antigens (1996), 48(3), 161-173
CODEN: TSANA2; ISSN: 0001-2815
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A monoclonal antibody (mAb), designated mNI-58A, was produced by immunizing mice with the lipopolysaccharide (LPS)-stimulated monocyte-like cell line, U937. The antigen defined by mNI-58A was widely expressed on various lymphoid cells and all cell lines examd. except the erythroid cell line, K562. When the reactive patterns between mNI-58A and the mAbs to various human differentiation antigens (CD11a, CD11b, CD11c, CD14, CD16, CD18, CD23, CD28, CD29, CD31, **CD43**, **CD44**, **CD45RA**, **CD50**, **CD54**, CD58, **CD80**, **CD102**, CD106, HLA-class I and -class II antigen) were compared, that of mNI-58A was similar to those of the leukocyte function-assocd. antigen-1 (LFA-1) mAbs. Using a competitive immunofluorescence binding assay it was found that the preincubation with one of the CD11a mAbs, 2F12 completely blocked the subsequent binding of mNI-58A. MNI-58A prevented the homotypic cell aggregation of the phorbol myristate acetate (PMA)-activated U937 cells (referred to as PMA-U937) and PMA-activated Epstein-Barr virus (EBV)-transformed B cell lines, B-85 and Mann. MNI-58A markedly induced the spread formation of the PMA-U937 cells following this blocking of the homotypic cell aggregation, whereas 2F12 did not under the same condition. The spread formation induced by mNI-58A was completely blocked by cytochalasin B (CyB), cytochalasin D (CyD), cycloheximide (CHX) or protein kinase C inhibitors, sphingosine and H-7. The U937 cells markedly adhered to the tumor necrosis factor-.alpha. (TNF-.alpha.)-stimulated human umbilical vein endothelial cells (HUVECs) and also to the extracellular matrix protein, fibronectin, but mNI-58A did not enhance or block these adhesion processes. MNI-58A pptd. two glycoproteins with mol. wt. 180 kDa and 95 kDa as detd. by SDS-PAGE anal., which were identical to the LFA-.alpha. (CD11a) and .beta. (CD18) chains of leukocyte integrin pptd. by the CD11a mAbs, resp. Sequential immunopptn. studies using the CD11a mAb (2F12) also indicate that mNI-58A recognizes an epitope on the

.alpha.-chain of the LFA-1 mol. The ability of mNI-58A to block the PMA-U937 cells and to induce the spread formation of these cells suggests that mNI-58A is a novel mAb reacting with an epitope on the .alpha.-chain of LFA-1 different from those recognized with the existing CD11a mAbs.

L12 ANSWER 15 OF 34 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:142192 CAPLUS
DOCUMENT NUMBER: 124:173443
TITLE: Methods for inhibiting antigen specific T cell responses
INVENTOR(S): Blazar, Bruce R.; Vallera, Daniel A.
PATENT ASSIGNEE(S): Regents of the University of Minnesota, USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9534320	A2	19951221	WO 1995-US7351	19950607 <--
WO 9534320	A3	19960118		
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2191733	AA	19951221	CA 1995-2191733	19950607 <--
AU 9527018	A1	19960105	AU 1995-27018	19950607 <--
EP 784482	A2	19970723	EP 1995-922279	19950607
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10501815	T2	19980217	JP 1995-502351	19950607
AU 9947458	A1	19991028	AU 1999-47458	19990908

PRIORITY APPLN. INFO.: US 1994-255267 19940607
US 1995-472697 19950606
AU 1995-27018 19950607
WO 1995-US7351 19950607

AB Methods for inhibiting antigen-specific T cell responses by use of an agent which inhibits a costimulatory signal in T cells are disclosed. Preferably, both a first agent which inhibits a costimulatory signal in the T cell and a second agent which inhibits adhesion of the T cell to a cell presenting antigen to the T cell, are used to inhibit antigen-specific T cell responses. For example, anti-LFA-1 antibody, that inhibits adhesion of a T cell to a cell presenting antigen, can be used in conjunction with a CTLA4-Ig fusion protein which inhibits a costimulatory signal in the T cell. Alternatively, another agent which inhibits a costimulatory signal in T cells, such as an anti-**B7-1** antibody or an anti-B7-2 antibody can be used with a second agent which inhibits a proliferative signal in the T cell e.g., an anti-IL-2 receptor antibody. The methods of the invention are particularly useful for inhibiting graft vs. host disease and for inhibiting rejection of a transplanted tissue or organ.

L12 ANSWER 16 OF 34 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:113374 CAPLUS
DOCUMENT NUMBER: 124:143577
TITLE: Methods using FcR bridging compounds for the selective modulation of antigen-specific T-cell responsiveness
INVENTOR(S): De Boer, Mark; Barcy, Serge
PATENT ASSIGNEE(S): Innogenetics N.V., Belg.
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9532734	A1	19951207	WO 1995-EP2012	19950526 <--
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
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AU 9526709	A1	19951221	AU 1995-26709	19950526 <--
EP 759782	A1	19970305	EP 1995-921760	19950526
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				

PRIORITY APPLN. INFO.: EP 1994-870088 19940526
WO 1995-EP2012 19950526

AB The present invention relates to new Fc.gamma.RII bridging compns. for impairing the capacity of antigen presenting cells (APCs) to stimulate the activation of antigen-specific T-cells, resulting in modulation of antigen-specific T-cell responsiveness. More particularly, said Fc.gamma.RII bridging agents are chosen from the group consisting of: aggregated human IgG mols.; aggregated Fc fragments of human IgG mols.; a bivalent monoclonal antibody to the Fc.gamma.RII; a multivalent monoclonal antibody to the Fc.gamma.RII; a functionally active fragment of said bivalent or multivalent monoclonal antibody; a recombinant fusion protein of 2 or more human IgG Fc parts; liposome vesicles comprising any of the foregoing, provided that said Fc.gamma.RII compn. prevents the expression of the co-stimulatory mols. **B7-1**/2 and/or down modulates the **ICAM**-3 mol. expression by these professional APCs. The present invention also relates to prophylactic and therapeutic methods and compns. to prevent or treat the rejection of solid organs, tissues and cells after transplantation; for inducing T-cell anergy or T-cell tolerance; for treating allergic diseases; or for the treatment of autoimmune diseases. The present invention also relates to Fc.gamma.RII bridged professional APCs prepd. by bridging APCs with an Fc.gamma.RII bridging agent according to the present invention. In example, FcR bridging strongly down-modulated expression of **B7-1**, B7-2, CD14, **ICAM**-3 and strongly up-regulated expression of **CD44**. FcR bridging greatly inhibited secretion of interleukin 2, stimulation of resting T cells by monocytes, interaction of B7-1/CD28, proliferation of antigen-specific T cells, etc.

L12 ANSWER 17 OF 34 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 9
ACCESSION NUMBER: 1995:957728 CAPLUS
DOCUMENT NUMBER: 124:6596
TITLE: Dendritic cells generated from peripheral blood transfected with human tyrosinase induce specific T cell activation

AUTHOR(S): Alijagic, Selma; Moeller, Peter; Artuc, Metin; Jurgovsky, Klaus; Czarnetzki, Beate M.; Schadendorf, Dirk
CORPORATE SOURCE: Dep. Dermatol., Humboldt Univ. Berlin, Berlin, Germany
SOURCE: Eur. J. Immunol. (1995), 25(11), 3100-7
CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Peptides of melanosomal proteins have recently been shown to be recognized in an HLA-restricted mode by specific cytolytic T lymphocytes in melanoma patients. Dendritic antigen-presenting cells (DC) are considered to be the most effective stimulators of T cell responses, and the use of these cells has therefore been proposed to generate therapeutic responses to tumor antigens in cancer patients. The authors, therefore, generated DC from peripheral blood of normal donors in the presence of granulocyte/macrophage colony-stimulating factor and interleukin-4. Flow cytometric anal. of the cells during a 2-wk culture revealed a loss of CD14 and CD34 expression, a concomitant increase of CD1a, CD11a, b, and c, **CD44**, **CD45**, **CD54**, HLA-class I and II, and intermediate levels of CD26, **CD80**, and CD86. Cultured DC stimulated proliferation of allogeneic T cells and induced a marked, up to 20-fold, stimulation of T cell proliferation after pulsing with tetanus toxoid. To achieve independence of already-identified antigenic peptides presented in HLA class I-restricted fashion, which limits the general applicability of such peptides for vaccination of melanoma patients, the authors tested whether DC are transfectable with eukaryotic expression plasmids. DC transfected with 2 reporter genes (CAT, .beta.-galactosidase) using a liposome-based transfection technique, exhibited only low levels of enzymically active proteins, but were able to degrade rapidly intracellular proteins and to process peptides efficiently. Chloramphenicol acetyltransferase as well as tyrosinase mRNA were detectable after transfection by reverse transcriptase-PCR, and enzyme activities became measurable. Furthermore, DC transfected with the tyrosinase gene were able to induce specific T cell activation in vitro, indicating appropriate peptide processing and presentation in DC after transfection. These data suggest new approaches to future tumor vaccination strategies.

L12 ANSWER 18 OF 34 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 10
ACCESSION NUMBER: 1995:718947 CAPLUS
DOCUMENT NUMBER: 123:141663
TITLE: Shigella infection induces cellular activation of T and B cells and distinct species-related changes in peripheral blood lymphocyte subsets during the course of the disease
AUTHOR(S): Islam, Dilara; Bardhan, Pradeep Kumar; Lindberg, Alf A.; Christensson, Birger
CORPORATE SOURCE: Dep. Immunol., Huddinge Univ. Hosp., Huddinge, Swed.
SOURCE: Infect. Immun. (1995), 63(8), 2941-9
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Immunophenotypic changes in peripheral blood lymphocytes (T, B, and NK cells) in patients during shigellosis was characterized by using triple-color flow cytometry. Eleven Shigella dysenteriae 1-infected adult patients (SDIP), 11 Shigella flexneri-infected adult patients (SFIP), 15 age- and sex-matched healthy controls from Bangladesh (C-B), and 15 healthy volunteers from Sweden (V-S) were studied. In SDIP and SFIP, a significant increase in the **CD45RO**+ cells in both **CD4**+ and CD8+ T cells was seen. We found evidence for sequential T-cell activation, as shown by increased proportions of CD25 and **CD4**+ cells; HLA-DR and CD38 on CD8+ cells, and **CD54** on **CD4**+ and CD8+ cells. We found differences in the lymphocyte activation and subset patterns related to the infecting Shigella species. Thus, a decrease in **CD45** expression was seen in SFIP; this decrease progressed further during the disease. The proportions of NK cells (CD56+ cells) and CD3- CD8+ cells out of the total CD8+ cells were increased in SFIP but not in SDIP. The CD3+ CD8+ CD57+ T-cell subset was significantly lower in SDIP than in C-B. The proportion of B-lymphocyte-expressing activation markers **CD80** and CD23 was higher in patients than in C-B. There was a significant increase in the proportion of **CD4**+ T cells and a significant decrease in the percentages of total B cells, the CD3+ CD8+ CD57+ T-cell subset, and the CD56+ CD16+ NK-cell subset for V-S compared with C-B. Our results indicate that distinct subset changes and activation patterns are elicited in SDIP compared with SFIP and also that the degree of activation is related to disease severity. In addn., a common sequence of cell activation was seen during the disease course. The difference in the subset patterns seen in C-B and V-S may be related to differences in the levels or spectra of infectious agents in the environment.

L12 ANSWER 19 OF 34 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 11
ACCESSION NUMBER: 1995:840493 CAPLUS
DOCUMENT NUMBER: 123:254196
TITLE: Differential effects of interleukin-10 on the expression of HLA class II and CD1 molecules induced by granulocyte/macrophage colony-stimulating factor/interleukin-4
AUTHOR(S): Thomssen, Henrike; Kahan, Melvyn; Londei, Marco
CORPORATE SOURCE: Kennedy Inst. Rheumatol., London, W6 8LW, UK
SOURCE: Eur. J. Immunol. (1995), 25(9), 2465-70
CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Interleukin (IL)-10 down-regulates HLA class II mols., whether constitutively expressed or up-regulated by interferon-.gamma. or IL-4 on monocytes but not on B lymphocytes. In this study the authors show that IL-10 does not inhibit HLA class II expression induced by the combination granulocyte/macrophage colony-stimulating factor and IL-4 on monocytes, although it simultaneously abrogates the expression of CD1 mols. induced by the same combination of cytokines. CD1 mols. can act as element of genetic restriction for **CD4**- CD8-T lymphocytes, and the suppression of CD1 expression by IL-10 abolished antigen presentation to CD1-restricted **CD4**- CD8-T cell receptor-pos. T cells. Although HLA class II expression was not down-regulated by IL-10, the antigen specific proliferative response of **CD4**+ T cells was nevertheless decreased. This was not caused by down-regulation of known co-stimulatory mols. such as **B7.1**, B7.2 and **ICAM**-1. IL-10 decreased the antigen specific proliferative response further by directly influencing the T lymphocytes. The results indicate that IL-10 exerts some of its immunoregulatory functions by differential modulation of antigen presenting mols., induced by the same combination of cytokines.

L12 ANSWER 20 OF 34 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 12
ACCESSION NUMBER: 1995:766933 CAPLUS
DOCUMENT NUMBER: 123:167576
TITLE: Establishment of a cell line with features of early dendritic cell precursors from fetal mouse skin
AUTHOR(S): Girolomoni, Giampiero; Lutz, Manfred B.; Pastore, Saveria; Assmann, Caroline U.; Cavani, Andrea; Ricciardi-Castagnoli, Paola
CORPORATE SOURCE: Lab. of Immunology, Inst. Dermopatico dell'Immacolata, Rome, Italy
SOURCE: Eur. J. Immunol. (1995), 25(8), 2163-9
CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English
AB During ontogeny, the skin is progressively populated by major histocompatibility complex class II-neg. dendritic cell (DC) precursors that then mature into efficient antigen-presenting cells (APC). To characterize these DC progenitors better, we generated myeloid cell lines from fetal mouse skin by infecting cell suspensions with a retroviral vector carrying an envAKR-mycMH2 fusion gene. These cells, represented by the line FSDC, displayed a dendritic morphol. and their proliferation in serum-free medium was promoted by granulocyte/macrophage colony-stimulating factor (GM-CSF), but not by macrophage-CSF. FSDC expressed strong surface-membrane ATP/ADPase activity, intracellular staining for 2A1 antigen, and a surface phenotype consistent with a myeloid precursor: H-2d,b+, I-Ad,b+, **CD54**+, CD11b+, CD11c+, 2.4G2+, F4/80+, **CD44**+, 2F8+, ER-MP 12-, Sca-1+, Sca-2+, NLDC-145-, B7.2+, **B7**.,1-, J11d-, B220-, Thy-1-, and CD3-; FSDC stimulated poorly allogeneic or syngeneic T cells in the primary mixed-leukocyte reaction, and markedly increased this function after treatment with GM-CSF, GM-CSF and interleukin (IL)-4 or interferon-.gamma. (IFN-.gamma.); in contrast, stem cell factor, IL-1.alpha. and tumor necrosis factor-.alpha. had no effect. Preculture with IFN-.gamma. was required for presentation of haptens to primed T cells in vitro. However, FSDC, even after cytokine activation, were less potent APC than adult epidermal Langerhans cells in both of the above assays. Finally, FSDC derivatized with haptens and injected either i.v. or s.c. could efficiently induce contact sensitivity responses in naive syngeneic mice. The results indicate that fetal mouse skin is colonized by myeloid precursors possessing a macrophage/immature DC-like surface phenotype and priming capacity in vivo. These cells need further differentiation and activation signals (e.g. cytokines) to express their antigen presenting potential in vitro.

L12 ANSWER 21 OF 34 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 13
ACCESSION NUMBER: 1995:692473 CAPLUS
DOCUMENT NUMBER: 123:109667
TITLE: Mechanism of enhanced antigen presentation by B cells activated with anti-.mu. plus interferon-.gamma.: role of B7-2 in the activation of naive and memory **CD4**+ T cells
AUTHOR(S): Morokata, Tatsuaki; Kato, Takuma; Igarashi, Osamu; Nariuchi, Hideo
CORPORATE SOURCE: The Institute of Medical Science, The University of Tokyo, Tokyo, 108, Japan
SOURCE: Eur. J. Immunol. (1995), 25(7), 1992-8
CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English
AB B cells activated with anti-.mu. antibody plus interferon (IFN)-.gamma. exerted strong antigen presenting activity for T cell proliferation. The enhanced antigen presentation function was shown to be due to the increase in B7-2 expression. When B cells were stimulated with anti-.mu., expression of MHC major histocompatibility complex class II, heat-stable antigen (HSA), **ICAM**-1, and B7-2 was increased. The presence of IFN-.gamma. further augmented the expression of B7-2 on anti-.mu.-stimulated B cells. **B7**-1 was not expressed on B cells under these conditions. The participation of B7-2 in the elicitation of the proliferative response of T cells was confirmed by the inclusion of anti-B7-2 antibody in cultures. The enhanced expression of either HSA or **ICAM**-1 was shown not to play a major role in the increased B cell antigen presentation capacity. The major T cell population responding to this activated B cell antigen presentation was shown to be **CD44low** naive **CD4**+ T cells, whereas **CD45RBlow** memory **CD4**+ T cells responded only weakly. The difference in proliferative responses between naive and memory **CD4**+ T cells was explained by the different efficiency in IL-2 prodn. of these cell populations in response to antigen presentation by B cells activated by anti-.mu. plus IFN-.gamma.. Thus, IFN-.gamma. plays an important role in recruitment of naive T cells for an immune response.

L12 ANSWER 22 OF 34 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 14
ACCESSION NUMBER: 1996:122224 CAPLUS
DOCUMENT NUMBER: 124:200004
TITLE: Bone marrow-derived dendritic cell progenitors (NLDC 145+, MHC class II+, B7-1dim, B7-2-) induce alloantigen-specific hyporesponsiveness in murine T lymphocytes
AUTHOR(S): Lu, Lina; McCaslin, Delbert; Starzl, Thomas E.; Thomson, Angus W.
CORPORATE SOURCE: Pittsburgh Transplantation Institute, University Pittsburgh, Pittsburgh, PA, 15213, USA
SOURCE: Transplantation (1995), 60(12), 1539-45
CODEN: TRPLAU; ISSN: 0041-1337
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The functional maturation of dendritic cells (DC) and other antigen-presenting cells is believed to reflect the upregulation of cell surface major histocompatibility complex (MHC) class II and other T cell costimulatory mols., esp. the CD28 ligands **B7**-1 (**CD80**) and B7-2 (CD86). In this study, we propagated cells exhibiting characteristics of DC precursors from the bone marrow (BM) of B10 mice (H-2b; I-A+) in response to granulocyte-macrophage colony stimulating factor (GM-CSF). The methods used were similar to those employed previously to propagate DC progenitors from normal mouse liver. Cells expressing DC lineage markers (NLDC 145+, 33D1+, N418+) harvested from 8-10-day GM-CSF stimulated BM cell cultures were **CD45**+, heat-stable antigen+, **CD54**+, **CD44**+, MHC class II+, B7-1dim but B7-2- (costimulatory mol.-deficient). Supplementation of cultures with interleukin-4 (IL-4) in addn. to GM-CSF however, resulted in marked upregulation of MHC class II and B7-2 expression. These latter cells exhibited potent allostimulatory activity in primary mixed leukocyte cultures. In contrast, the cells stimulated with GM-CSF alone were

relatively weak stimulators and induced alloantigen-specific hyporesponsiveness in allogeneic T cells (C3H; H-2k; I-E+) detected upon restimulation in secondary MLR. This was assocd. with blockade of IL-2 prodn. Reactivity to third-party stimulators was intact. The hyporesponsiveness induced by the GM-CSF stimulated, costimulatory mol.-deficient cells was prevented by incorporation of anti-CD28 monoclonal antibody in the primary MLR and was reversed by addn. of IL-2 to restimulated T cells. The findings show that MHC class II+ B7-2- cells with a DC precursor phenotype can induce alloantigen-specific hyporesponsiveness in vitro. Under the appropriate conditions, such costimulatory mol.-deficient cells could contribute to the induction of donor-specific unresponsiveness in vivo.

L12 ANSWER 23 OF 34 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 15
ACCESSION NUMBER: 1995:820330 CAPLUS
DOCUMENT NUMBER: 123:225399
TITLE: The primary alloresponse of human CD4+ T cells is dependent on B7 (CD80), augmented by CD58, but relatively uninfluenced by CD54 expression
AUTHOR(S): Hargreaves, Roseanna; Logiou, Vassiliki; Lechler, Robert
CORPORATE SOURCE: Department of Immunology, Royal Postgraduate Medical School, London, W12 0NN, UK
SOURCE: Int. Immunol. (1995), 7(9), 1505-13
CODEN: INIMEN; ISSN: 0953-8178
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Conflicting data have been reported regarding the relative abilities of B7, ICAM-1 and LFA-3 to provide co-stimulation for the induction of a primary T cell alloproliferative response. A series of naturally HLA-DR-expressing cell lines and panels of human and murine transfectants expressing DR alloantigens in conjunction with combinations of mouse or human B7.1, human LFA-3 and human ICAM-1 were used to analyze the contributions of these mols. to primary alloproliferative responses by adult and cord blood CD4+ T cells. The results demonstrated that B7 expression is required, and may be sufficient for the induction of a primary alloresponse. The allostimulation obsd. in response to DR-expressing murine DAP.3 cells, that constitutively express B7.1, was inhibited by the presence of the murine cytolytic T lymphocyte-assocd. antigen 4-human Fc.gamma.1 fusion protein, suggesting that mouse B7.1 provides sufficient co-stimulation for a primary human alloproliferative response. Expression of supranormal levels of human B7. 1 on the allostimulator cells led to a redn. in the proliferative response, suggesting that an optimal level of B7 exists which, if exceeded, leads to inhibition. Co-expression of LFA-3 with B7. 1 by the allostimulator cells caused a marked increase in the proliferative response. Expression of ICAM-1 had relatively little effect. No differences were seen in the co-stimulatory requirements of naive cord blood vs. CD45RO adult T cells. These results highlight the key mol. interactions that govern immunogenicity with relevance to inhibiting unwanted immune responses to transplanted tissues and providing anti-tumor immunity.

L12 ANSWER 24 OF 34 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 16
ACCESSION NUMBER: 1995:744646 CAPLUS
DOCUMENT NUMBER: 123:138647
TITLE: Human immature thymocytes as target cells of the leukemogenic activity of human T-cell leukemia virus type I
AUTHOR(S): Maguer-Satta, Veronique; Gazzolo, Louis; Duc Dodon, Madeleine
CORPORATE SOURCE: Immuno-Viologie Moleculaire et Cellulaire, Centre National Recherche Scientifique, Universite Claude Bernard, Lyon, Fr.
SOURCE: Blood (1995), 86(4), 1444-52
CODEN: BLOOAW; ISSN: 0006-4971
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The risk of developing adult T-cell leukemia (ATL) assocd. with neonatal infection by human T-cell leukemia virus type I (HTLV-I) suggests that early events triggered by HTLV-I might be of crucial importance in initiating the multistep lymphoproliferative process leading several decades later to the development of leukemic disease. Thus, infection of thymocytes early in life might be directly correlated with the development of ATL. In the present study, we show that in vitro infection of mature (CD2+CD3+ or immature (CD2+CD3-) thymocytes resulted in the exogenous interleukin (IL)-2-dependent proliferation of HTLV-I-pos. thymocytes, most of them displaying a CD2+CD31-CD4+ pheno-type and expressing the CD25 mol., the .alpha. chain of the IL-2 receptor. Furthermore, the CD80 and CD54 antigens, normally expressed by thymic stromal cells, were detected on these transformed thymocytes, indicating that HTLV-I-infection may disturb the cooperation between thymocytes and their thymic environment. These HTLV-I-pos. thymocytes were producing significant amts. of IL-6, which was found to be implicated in their proliferation and in the expression of CD25, as demonstrated by blocking expts. using monoclonal antibody to IL-6. The present study suggests that immature thymocytes may provide an environment favorable to the unfolding of events leading to leukemia.

L12 ANSWER 25 OF 34 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 17
ACCESSION NUMBER: 1995:757338 CAPLUS
DOCUMENT NUMBER: 123:225838
TITLE: CD86 (B70/B7-2) on endothelial cells co-stimulates allogeneic CD4+ T cells
AUTHOR(S): Seino, Kenichiro; Azuma, Miyuki; Bashuda, Hisashi; Fukao, Katashi; Yagita, Hideo; Okumura, Ko
CORPORATE SOURCE: Dep. Immunol., Juntendo Univ. Sch. Med., Bunkyo, 113, Japan
SOURCE: Int. Immunol. (1995), 7(8), 1331-7
CODEN: INIMEN; ISSN: 0953-8178
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In vascularized organ transplantation, vascular endothelial cells (EC) confronting recipient T cells are potentially significant APC initiating cellular immune responses that lead to rejection. In the present study, we studied the ability of human EC to stimulate allogeneic T cells and the co-stimulatory mols. involved in this response. On both human umbilical vein endothelial cells (HUVEC) and microvascular endothelial cells (MVEC), MHC class I, intercellular adhesion mol. (ICAM)-1 and CD86 were constitutively expressed as assessed by flow cytometry. After IFN-.gamma. treatment, MHC class II expression was induced, and MHC class I and

ICAM-1 were up-regulated. In contrast, the expression of CD86 was unchanged and CD80 was undetectable even after IFN-.gamma. treatment. Highly purified CD4+ T cells proliferated in response to IFN-.gamma.-treated allogeneic HUVEC and MVEC, and this response was efficiently blocked by mAb to MHC class II, ICAM-1 and CD86. Furthermore, the addn. of anti-CD86 mAb to the primary culture with allogeneic EC resulted in the induction of alloantigen-specific anergy. These results suggest that CD86 expressed on EC plays a crit. role in initiating cellular immune responses to vascularized allografts and would be an important target for immune intervention.

L12 ANSWER 26 OF 34 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 18
ACCESSION NUMBER: 1995:609251 CAPLUS
DOCUMENT NUMBER: 123:31143
TITLE: Co-expression of B7-1 and ICAM-1 on tumors is required for rejection and the establishment of a memory response
AUTHOR(S): Cavallo, Federica; Martin-Fontecha, Alfonso; Bellone, Matteo; Heltai, Silvia; Gatti, Evelina; Tornaghi, Paola; Freschi, Massimo; Forni, Guido; Dellabona, Paolo; Casorati, Giulia
CORPORATE SOURCE: CNR Immunogenetica e Oncologia Sperimentale, Universita di Torino, Italy
SOURCE: Eur. J. Immunol. (1995), 25(5), 1154-62
CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Although the transfection of B7-1 cDNA into a few mouse tumor cell lines can induce anti-tumor T cell immunity, its expression alone is ineffective in many other tumor cell lines tested. We were interested to study what factors limit B7-1 co-stimulatory activity, and decided to investigate whether B7-1 requires the cooperation of ICAM-1 to provide the minimal co-stimulatory signal fro establishing an efficient anti-tumor immunity. We show that the transfection of B7-1 cDNA into three ICAM-1+ (plasmacytoma J558L, T lymphomas EL-4 and RMA), but not into two ICAM-1- tumor cell lines (adenocarcinoma TS/A and melanoma B16.F1), is sufficient to induce their complete rejection in syngeneic mice. The expression of ICAM-1 is necessary for the rejection of the B7 expressing tumors, since the primary response elicited by B7-1+ EL-4 and RMA clones expressing reduced levels of ICAM-1 is severely reduced. Furthermore, super-transfection of ICAM-1 cDNA into B7-1+ adenocarcinoma and melanoma clones optimizes their primary rejection. Histol. examn. of transfected tumors reveals that B7-1 and ICAM-1 exert a potent pro-inflammatory activity. The intra-tumor infiltration is composed of both eosinophils and lymphomonocytes, and is already massive 5 days after the tumor challenge. The primary rejection of the B7-1+ ICAM-1+ tumors depends critically on CD8+ T cells, natural killer cells and granulocytes, but is independent of CD4+ T cells. Remarkably, in addn. to its effects on the early phases of the immune response, the co-expression of ICAM-1 and B7-1 on tumors is also necessary for the efficient induction of a memory response. In fact, only the primary challenge with B7=1+, ICAM-1+ tumor cells protects the majority of the mice from a second injection of parental tumor cells. Collectively, our findings indicate that B7-1 and ICAM-1 are fundamental components for triggering the primary injection of tumors and establishing a protective memory response. These findings may help to define new strategies for the rational application of co-stimulation in tumor immunotherapy.

L12 ANSWER 27 OF 34 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 19
ACCESSION NUMBER: 1995:682349 CAPLUS
DOCUMENT NUMBER: 123:81465
TITLE: Rapid development of murine AIDS is dependent on signals provided by CD54 and CD11a
AUTHOR(S): Makino, Masahiko; Yoshimatsu, Kazuhiko; Azuma, Miyuki; Okada, Yoshiaki; Hitoshi, Yasumichi; Yagita, Hideo; Takatsu, Kiyoshi; Komuro, Katsutosni
CORPORATE SOURCE: Dep. Bact. Blood Prod., Natl. Inst. Health Japan, Tokyo, Japan
SOURCE: J. Immunol. (1995), 155(2), 974-81
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Murine AIDS (MAIDS) is induced by infection with the replication-defective virus (BM5def) component in the LP-BM5 murine leukemia virus (MuLV) mixt. The disease is characterized by polyclonally activated CD4+ T cells and B cells. It is known that BM5def is expressed at highest levels in B lymphocytes and that B cells serve as viral antigen-presenting cells. Full and sustained activation of CD4+ T cells against a conventional antigen (Ag) usually requires both TCR and costimulating signals. Among various mols. known to provide costimulatory function, the expression of CD54 (ICAM-1) and CD11a/CD18 (LFA-1) on MAIDS B cells was increased, whereas that of CD2, heat-stable Ag (CD24), CD80 (B7-1), and CD86 (B7-2) was unchanged from normal. C57BL/6 mice depleted of both CD54 and CD11a expression as a result of chronic administration of mAb developed no MAIDS at 4 wk and 8 wk after LP-BM5 MuLV infection. In addn., the proliferative response of B cells to mitogen was well conserved, whereas MAIDS-assocd. increases in serum Ig levels were inhibited. Replication of BM5def was suppressed markedly in infected mice treated with the CD54 and CD11 a mAbs. Thus, the CD54/CD11a signal transduction pathway is a crit. determinant of MAIDS development, and the lack of an immune response against viral Ag is enough to suppress BM5def replication and to prevent MAIDS.

L12 ANSWER 28 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 20
ACCESSION NUMBER: 95366159 EMBASE
DOCUMENT NUMBER: 1995366159
TITLE: Dendritic antigen-presenting cells from the peripheral blood of renal-cell-carcinoma patients.
AUTHOR: Radmayr C.; Bock G.; Hobisch A.; Klocker H.; Bartsch G.; Thurnher M.
CORPORATE SOURCE: Department of Urology, University of Innsbruck, Anichstrasse 35,6020 Innsbruck, Austria
SOURCE: International Journal of Cancer, (1995) 63/5 (627-632).
ISSN: 0020-7136 CODEN: IJCNAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 016 Cancer
025 Hematology
026 Immunology, Serology and Transplantation
028 Urology and Nephrology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Dendritic cells are considered to be the initiators of immune responses, including those directed against tumors. Clinical research on dendritic cells was long hampered by the limited availability of these cells. The recent identification of cytokine combinations that mobilize dendritic cells with potent antigen-presenting cell function from peripheral blood represented a major progress, We show in this study that substantial numbers of dendritic cells can be obtained from the peripheral blood of patients with renal-cell carcinoma The procedure requires a relatively small blood sample (40 ml) and avoids both priming of the patient with granulocyte-colony stimulating factor and leukapheresis. Approximately 2 to 8 million cells with the characteristics of dendritic cells could be obtained: phase-contrast microscopy revealed the typical cytoplasmic processes or veils; phenotypic analysis confirmed expression of dendritic-cell-associated molecules, including MHC class II, CD1a, **CD4**, **ICAM**-1 (**CD54**), LFA-3 (CD58), B7-1 (**CD80**) and B7-2 (CD86), and absence of T-cell, B-cell and monocyte markers; in addition, these cells rapidly attached to and migrated on collagen-type-1 coated surfaces. Interestingly, attachment was accompanied by acquisition of the CD14 antigen; functionally, cultured dendritic cells proved to be very potent co-stimulators of the phytohemagglutinin-induced proliferation of autotogous tumor-infiltrating lymphocytes. The reproducible growth of functional dendritic cells from cancer patients is encouraging for the design of immunotherapy protocols.

L12 ANSWER 29 OF 34 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:708247 CAPLUS
DOCUMENT NUMBER: 123:109557
TITLE: Adhesion molecules in immune tolerance
AUTHOR(S): Bashuda, Hisashi
CORPORATE SOURCE: Sch. Med., Juntendo Univ., Tokyo, 113, Japan
SOURCE: Ensho to Men'eki (**1995**), 3(4), 355-60
CODEN: ENMEFA; ISSN: 0918-8371
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review, with 15 refs., on the adhesion mols. as costimulatory signal transduction mols. on antigen presenting cells (APC), and results of prolongation of graft survival by blocking of the function of adhesion mols. (LFA-1/**ICAM**-1 system CD28, CTLA-4/**CD80** and CD88 system, CD2/**CD48** system, CD2/**CD48** system, and VLA-4/VCAM-1 system). The mechanisms of rejection suppression are discussed.

L12 ANSWER 30 OF 34 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 21
ACCESSION NUMBER: 1995:407851 CAPLUS
DOCUMENT NUMBER: 122:158092
TITLE: CD28 functions as an adhesion molecule and is involved in the regulation of human IgE synthesis
AUTHOR(S): Life, Paul; Aubry, Jean-Pierre; Estoppey, Sandrine; Schnuriger, Valerie; Bonnefoy, Jean-Yves
CORPORATE SOURCE: Glaxo Inst. Molecular Biol., Geneva, Switz.
SOURCE: Eur. J. Immunol. (**1995**), 25(2), 333-9
CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Activated T cells induce IgE switching in B cells via a combination of lymphokines and direct T:B cell contact. As CD28-deficient mice have reduced basal levels of IgG1 and IgG2a and diminished Ig class switching, the authors investigated whether the CD28/**B7.1** (**CD80**) ligand pairing might also be involved in human IgE regulation. Co-incubation of an allergen-specific, human T cell clone with tonsillar B cells caused a marked up-regulation of CD28 expression, whereas, in contrast, **CD45RB** expression was unaffected. To test whether blocking the CD28:**B7.1** interaction affected IgE synthesis, a dialyzed anti-CD28 monoclonal antibody (mAb) was added to cultures contg. tonsillar B cells, pre-activated T cell clones, and interleukin-4. Anti-CD28 treatment caused a reproducible, dose-dependent inhibition of IgE, but not IgG synthesis that was accompanied by a visible decrease in cell aggregate formation. Conversely, an anti-**B7**.1 mAb had no effect in this system. The effect of blocking CD28-ligand interactions on lymphocyte adhesion was formally assessed on human T cell clones and B cell lines using dual intracellular staining and flow cytometry. Co-incubation with an anti-CD28 mAb, but not control IgG or anti-**B7.1** mAb, resulted in a marked impairment of conjugate formation that correlated well with T cell surface expression of CD28. Using this system the authors found that an anti-CTLA-4 mAb but not an anti-B7.2 mAb inhibited T:B cell conjugate formation. Lastly, in addn. to a direct effect of anti-CD28 mAb on conjugate formation, 14-day culture of T and B cells in the presence of anti-CD28 caused a marked decrease of **ICAM**-1 (**CD54**) expression on aggregated lymphocytes. In contrast, LFA-1 (CD18) expression was unaffected. Thus, the T cell co-stimulatory mol. CD28 is involved in the regulation of IgE synthesis in vitro. CD28 may act to a limited extent as an adhesion mol., though apparently not by pairing with **B7.1** or B7.2. It is more likely that ligation of CD28 under certain conditions modulates the expression of other T and B cell surface mols.

L12 ANSWER 31 OF 34 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 22
ACCESSION NUMBER: 1995:694498 CAPLUS
DOCUMENT NUMBER: 123:106613
TITLE: Hydrogen peroxide mediates UV-induced impairment of antigen presentation in a murine epidermal-derived dendritic cell line
AUTHOR(S): Caceres-Dittmar, Gisela; Ariizumi, Kiyoshi; Xu, Shan; Tapia, Felix J.; Bergstresser, Paul R.; Takashima, Akira
CORPORATE SOURCE: Dep. Dermatology, Univ. Texas Southwestern Med. Cent., Dallas, TX, 75235, USA
SOURCE: Photochem. Photobiol. (**1995**), 62(1), 176-83
CODEN: PHCBAP; ISSN: 0031-8655
DOCUMENT TYPE: Journal
LANGUAGE: English
AB UV-B (290-320 nm) radiation is known to impair the antigen-presenting cell (APC) function of Langerhans cells (LC), skin-specific members of the dendritic cell (DC) family. We sought to address mechanisms of this effect, focusing on the role played by hydrogen peroxide. For this purpose, we used a newly established murine DC line, XS52, which resemble epidermal LC in several respects. The APC capacity of XS52 cells, using

two different CD4+ T cell clones as responders, was inhibited significantly (>50%) by exposure to UV radiation (unfiltered FS20 sunlamps) at relatively small fluences (50-100 J/m2). UV radiation also inhibited growth factor-dependent proliferation of XS52 cells. Cell surface phenotype was relatively well preserved after irradn.; expression levels of B7-1 and B7-2 were reduced slightly, while other mols. (e.g. Ia, CD54, CD11a and CD18) were not affected. With respect to the role played by hydrogen peroxide, pretreatment with purified catalase (900 U/mL) prevented UV-induced inhibition of APC function. Short-term exposure to 3 mM H2O2 or tert-Bu H2O2 mimicked UV radiation by inhibiting APC function. Finally, intrinsic catalase activity was substantially lower in XS52 cells compared with PAM 212 keratinocytes. These results indicate that the generation of hydrogen peroxide alone is sufficient to produce some, but not all, of the deleterious effects of UV radiation on DC derived from the skin.

L12 ANSWER 32 OF 34 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 23
ACCESSION NUMBER: 1995:656233 CAPLUS
DOCUMENT NUMBER: 123:81524
TITLE: Costimulatory requirements of naive CD4+ T cells. ICAM-1 or B7-1 can costimulate naive CD4 T cell activation but both are required for optimum response
AUTHOR(S): Dubey, Caroline; Croft, Michael; Swain, Susan L.
CORPORATE SOURCE: Dep. Biol., Univ. California, San Diego, La Jolla, CA, 92093, USA
SOURCE: J. Immunol. (1995), 155(1), 45-57
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Efficient initiation of a CD4 T cell response requires both activation through the TCR and costimulation provided by mols. on APC with counterreceptors on the T cell. We investigated the relative contribution of the ICAM-1:LFA-1 and B7:CD28/CTLA-4 costimulatory pathways in naive T cell activation, using either anti-CD28 Ab or fibroblast cell lines transfected with I-Ek, which express either no costimulatory mols., ICAM-1 alone, B7-1 alone, or ICAM-1 and B7-1 together. Peptide Ag or immobilized anti-CD3 was used to provide the TCR signal. CD4 T cells from mice transgenic for the V.beta.3/V.alpha.11 TCR, which recognize a peptide of pigeon cytochrome c complexed to I-Ek, were used as a source of naive T cells. Naive T cells stimulated with Ag or anti-CD3 responded well to high nos. of APC expressing either ICAM-1 alone or B7-1 alone. However, APC expressing both ICAM-1 and B7-1 were much better stimulators of proliferation and IL-2 secretion at low cell nos., and were far superior inducers of IL-2 at higher nos., indicating a synergy between the two pathways. Stimulation provided by ICAM-1 could not be solely attributed to adhesive strengthening of other pathways, since costimulation was seen when immobilized anti-CD3 was used and when ICAM-1 only APC were added, indicating that ICAM-1 was in fact acting as a classic costimulatory mol. Both the magnitude of the response and the amt. of costimulation required for response were dependent on the intensity of TCR interaction. These results suggest that an efficient naive T cell response requires both a strong TCR signal and more than one costimulatory signal that will synergize with the TCR signal. This offers an explanation as to why APC such as dendritic cells and activated B cells, which express high levels of multiple costimulatory/adhesion mols., are the only APC that elicit naive T cell responses.

L12 ANSWER 33 OF 34 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 24
ACCESSION NUMBER: 1995:514551 CAPLUS
DOCUMENT NUMBER: 122:312753
TITLE: B7-1 expression decreases tumorigenicity and induces partial systemic immunity to murine neuroblastoma deficient in major histocompatibility complex and costimulatory molecules
AUTHOR(S): Katsanis, Emmanuel; Xu, Zhiyi; Bausero, Maria A.; Dancisak, Betsy B.; Gorden, Keith B.; Davis, Geoffrey; Gray, Gary S.; Orchard, Paul J.; Blazar, Bruce R.
CORPORATE SOURCE: Department of Pediatrics, University of Minnesota, Minneapolis, MN, USA
SOURCE: Cancer Gene Ther. (1995), 2(1), 39-46
CODEN: CGTHEG; ISSN: 0929-1903
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Neuroblastoma may escape an immune attack by virtue of its low expression of surface accessory mols. essential in the antitumor response. Murine neuroblastoma, neuro-2a, was transduced with the retroviral vector LB7-1SN to examine the influence of B7-1 expression on the immune response directed against a low major histocompatibility class (MHC) I and class II neg., B7-2, and ICAM-1 neg. tumor. Using a retroperitoneal model for implantation of neuroblastoma in its natural site, the authors demonstrated that expression of B7-1 by neuro-2a reduces its tumorigenicity. Coinjection of B7-1-pos. and -neg. cells improved survival compared with mice receiving B7-1-neg. cells alone. This was dependent on the ratio of B7-1+ to B7-1- neuro-2a cells injected. CD8+ and not CD4+ T-cell depletion significantly increased tumor-induced mortality in syngeneic A/J mice, indicating that B7-1 decreases tumorigenicity primarily by direct costimulation of CD8+ T cells. Rejection of N-2a/B7-1 tumors or preimmunization with irradiated N-2a/B7-1 cells did not increase protection to challenge with unmodified neuro-2a cells over mice vaccinated with N-2a/neo. Furthermore, cytotoxic T lymphocyte (CTL) precursor frequencies were not significantly higher after in vivo priming and in vitro stimulation with irradiated N-2a/B7-1 compared with N-2a/neo, indicating that B7-1 costimulation by the tumor, in the absence of adequate antigen presentation by MHC mols., may limit the generation of effective CTLs.

L12 ANSWER 34 OF 34 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:633482 CAPLUS
DOCUMENT NUMBER: 123:31188
TITLE: Analysis of adhesion molecule-mediated signal transduction between T cells
AUTHOR(S): Wanibuchi, Masahiko; Murakami, Masaaki
CORPORATE SOURCE: Sch. Med., Sapporo Med. Univ., Japan
SOURCE: Sapporo Igaku Zasshi (1994), 63(5-6), 221-9
CODEN: SIZSAR; ISSN: 0036-472X
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB T cell activation requires engagement of the T cell receptor (TCR) with an immunogenic peptide bound to a major histocompatibility complex (MHC) mol. and a costimulatory signal provided by the antigen-presenting cell (APC). Although these events result in T cell clonal expansion, ligation of the TCR alone (lack of a costimulatory signal) does not stimulate T cell activation, but rather results in unresponsiveness known as T cell energy. Most investigations of the T cell activation mechanism have focussed on the system consisting of classical APC and T cells, but it is known that T cell can coexpress not only the adhesion mols. that provide costimulatory signals to T cells, but also their counter-receptors. In this paper, we analyze the role of adhesion mols. in T cell activation using a mouse **CD4**+ T cell clone, DB14. DB14 cells were able to proliferate upon stimulation of the TCR/CD3 complex alone either by appropriate MHC class II cDNA transfected CHO cells plus peptides or anti-CD3 monoclonal antibodies (mAb). Moreover the magnitude of anti-CD3 mAb-induced T cell proliferation was dependent on cell d., suggesting that cell to cell contact is important for the anti-CD3 mAb-induced DB cell proliferation. The DB14 cell expressed **B7-1**, CD28, **ICAM**-1 and LFA-1 mols. on its cell surface. Importantly, anti-CD3 mAb-induced proliferation was inhibited by CTLA-4 Ig or anti-LFA-1 mAb and the inhibitory effect of anti-LFA-1 mAb was stronger than that of CTLA-4 Ig. These results suggest that DB14 cells require two signals, the first, a TCR-mediated signal by anti-CD3 mAb and the second, a costimulatory signal through interaction of B7/CD28 and LFA-1/**ICAM**-1 pathways. Thus adhesion mols. on DB14 cells can provide a costimulatory signal for T cell proliferation, which suggests that T cells may provide costimulatory signals to each other at inflamed regions in vivo.

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(FILE 'HOME' ENTERED AT 10:03:54 ON 10 JUL 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 10:04:06 ON 10 JUL 2002

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L1         14884 S WEBB S?/AU OR WINGVIST O?/AU OR KARLSSON L?/AU OR JACKSON M?/
L2           198 S L1 AND CD4?
L3           185 S L2 NOT CD40
L4            14 S L2 AND (CD80 OR B7.1)
L5             7 DUP REM L4 (7 DUPLICATES REMOVED)
L6             5 S L5 AND (ICAM? OR CD54 OR CD50 OR CD102)
L7        233993 S CD4?
L8        217789 S L7 NOT CD40
L9          2210 S L8 AND (CD80 OR B7.1)
L10          322 S L9 AND (ICAM? OR CD54 OR CD50 OR CD102)
L11           72 S L10 AND PD<19960523
L12           34 DUP REM L11 (38 DUPLICATES REMOVED)
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=> s l12 and HIS?
L13 15 L12 AND HIS?

=> dis l13 1-15 ibib abs

L13 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:584820 CAPLUS
DOCUMENT NUMBER: 125:245461
TITLE: Immunogenicity of biliary epithelium: Investigation of antigen presentation to **CD4**+T cells
AUTHOR(S): Leon, Maria P.; Bassendine, Margaret F.; Wilson, Julia L.; Ali, Simi; Thick, Michael; Kirby, John A.
CORPORATE SOURCE: Medical School, University Newcastle upon Tyne, Newcastle upon Tyne, NE2 4HH, UK
SOURCE: Hepatology (Philadelphia) (1996), 24(3), 561-567
CODEN: HPTLD9; ISSN: 0270-9139
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The intrahepatic biliary epithelium is susceptible to extensive T-cell-mediated damage during primary biliary cirrhosis, primary sclerosing cholangitis, and hepatic allograft rejection. During these processes, human intrahepatic biliary epithelial cells (HIBEC) become activated and express high levels of the lymphocyte adhesion mols., intercellular adhesion mol.-1 (**ICAM**-1) and lymphocyte-assocd. antigen (LFA)-3, and of class II MHC antigens. It follows that activated HIBEC may also play a direct role in the activation of antigen-specific **CD4**+ T lymphocytes. The capacity of class II MHC antigen-expressing HIBEC to present antigen and induce specific proliferation of **CD4**+ T cells was examd. in this study. Lines of purified HIBEC were activated by culture with the proinflammatory cytokines interferon gamma (IFN-.gamma.) and tumor necrosis factor .alpha. and were mixed in coculture with allogeneic **CD4**+ T cells. The result of interaction between these cells was assessed by measurement of lymphoproliferation and IL-2 prodn. Class II MHC antigen-expressing HIBEC failed to induce either lymphoproliferation or IL-2 prodn. However, both of these parameters of T-cell activation were pos. in cocultures when a costimulation signal was delivered to T cells by adding bivalent anti-CD28 antibodies. The antigen-specific activation of these T cells was further enhanced by the addn. of a crosslinking secondary antibody that caused CD28 receptor aggregation. The failure of cytokine-stimulated HIBEC to induce T-cell activation is consistent with the observation that HIBEC do not express the costimulatory CD28 ligands **B7-1** or B7-2 at either mRNA or protein levels. It may be concluded that HIBEC are unlikely to play a direct role in activation of antigen-specific **CD4**+ T lymphocytes within the inflamed liver.

L13 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:504816 CAPLUS
DOCUMENT NUMBER: 125:165648
TITLE: Differing roles for B7 and intercellular adhesion molecule-1 in negative selection of thymocytes
AUTHOR(S): Kishimoto, Hidehiro; Cai, Zeling; Brunmark, Anders; Jackson, Michael R.; Peterson, Per A.; Sprent, Jonathan
CORPORATE SOURCE: Dep. Immunol., Scripps Res. Inst., La Jolla, CA, 92037., USA
SOURCE: J. Exp. Med. (1996), 184(2), 531-537
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To ensure self tolerance, immature thymocytes with high binding affinity for self peptides linked to major **histocompatibility** complex (MHC) mols. are eliminated in situ via apoptosis (neg. selection). The roles of two costimulatory mols., **B7-1** and intercellular adhesion mol.-1 (**ICAM**-1), in neg. selection was

examd. by studying apoptosis of T cell receptor transgenic CD4 +8+ thymocytes cultured with specific peptides presented by MHC class I-transfected Drosophila cells. When coexpressed on these cells, B7-1 and ICAM-1 act synergistically and cause strong class I-restricted neg. selection of thymocytes. When expressed sep., however, B7-1 and ICAM-1 display opposite functions: neg. selection is augmented by B7-1, but is inhibited by ICAM-1. It is notable that B7-1 is expressed selectively in the thymic medulla, whereas ICAM-1 is expressed throughout the thymus. Because of this distribution, the differing functions of B7-1 and ICAM-1 may dictate the sites of pos. and neg. selection. Thus, in the cortex, the presence of ICAM-1, but not B7-1, on the cortical epithelium may preclude or reduce neg. selection and thereby promote pos. selection. Conversely, the combined expression of B7-1 and ICAM-1 may define the medulla as the principal site of neg. selection.

L13 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:491349 CAPLUS
DOCUMENT NUMBER: 125:165520
TITLE: T-T cellular interaction between CD4-CD8- regulatory T cells and T cell clones presenting TCR peptide. Its implications for TCR vaccination against experimental autoimmune encephalomyelitis
AUTHOR(S): Kozovska, Milena F.; Yamamura, Takashi; Tabira, Takeshi
CORPORATE SOURCE: Dep. Demyelinating Dis. Aging, Natl. Cent. Neurol. Psychiatry, Kodaira, Japan
SOURCE: J. Immunol. (1996), 157(4), 1781-1790
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Regulatory T cells recognizing TCR determinants presumably play a crit. role in the control of exptl. autoimmune encephalomyelitis, a prototype tissue-specific autoimmune disease. This study was initiated to det. whether regulatory T cells can be induced against a V.beta.17a CDR2 peptide (residues 50-68) in SJL/J mice. Although the TCR peptide showed regulatory effects in vivo, the presence of T cells specific for the peptide could not be proven with conventional proliferation assays. Unexpectedly, in the presence of myelin basic protein-specific T clone cells (Tcc), the sensitized spleen cells vigorously proliferated in response to the TCR peptide. The subsequent expt. showed that this was due to the outstanding capability of the Tcc as APC for the exogenous TCR peptide. Using the Tcc as APC, the authors were able to establish V.beta.17a50-68-specific T cell lines from in vivo primed spleen cells. The line cells were MHC class I restricted and dominated by T cells with a distinct surface phenotype (CD4-CD8-V.beta.17a+). Presentation of the peptide by the Tcc was inhibited by treatment with gelonin that could block a MHC class I presentation pathway. The ability of T cells to present the TCR peptide was not related to their Ag specificity, but correlated with the expression levels of MHC class I mols. and adhesion mols. such as intercellular adhesion mol.-1 and B7-1 on their surface. The TCR peptide-specific T cells produced a sol. mediator(s) that is inhibitory for T cell activation and were protective against actively induced exptl. autoimmune encephalomyelitis. These results show that V.beta.17a50-68 vaccination induces regulatory CD4-CD8- T cells that could interact with T cells presenting relevant TCR fragments.

L13 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:450503 CAPLUS
DOCUMENT NUMBER: 125:140301
TITLE: Antigen-presenting-cell function of interferon .gamma.-treated human gingival fibroblasts
AUTHOR(S): Shimabukuro, Yoshio; Murakami, Shinya; Okada, Hiroshi
CORPORATE SOURCE: Faculty Dentistry, Osaka University, Suita, 565, Japan
SOURCE: J. Periodontal Res. (1996), 31(3), 217-228
CODEN: JPDRAY; ISSN: 0022-3484
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present study was carried out to examine the antigen-presenting cell (APC) functions of human gingival fibroblasts (HGF) elicited with IFN.gamma.. Stimulation of HGF with IFN.gamma. clearly induced HLA-DR expression and enhanced expression of intercellular adhesion mol.-1 (ICAM-1) on HGF. Despite the phenotypical resemblance of IFN.gamma.-treated HGF to so-called APC, HLA-DR pos. HGF were unable to induce proliferation of allo-reactive peripheral blood T cells (PBT) isolated from different donors. The failure of IFN.gamma.-treated HGF to stimulate unprimed allo-reactive PBT was not due to the lack of prodn. of IL-1 or the immunosuppressive effect of PGE2 from HGF. The fact that detectable expression of CD80, ligand for CD28, was not found on IFN.gamma.-treated HGF may at least in part explain the ineffective function of HGF as APC. Interestingly, IFN.gamma.-treated HGF induced proliferation of primed allo-reactive CD4+ T cells in a HLA-DR dependent manner, suggesting that IFN.gamma.-treated HGF may have the ability to stimulate pre-activated T cells. We then confirmed that high levels of IFN.gamma. mRNA were detectable in inflamed gingival tissue. Although it cannot be concluded from this study that HGF are incapable of effectively presenting antigenic peptides to autologous T cells bearing appropriate T cell receptors, present results suggest that HGF may be affected by locally-secreted IFN.gamma. and that the IFN.gamma.-stimulated HGF may play a role in regulating immune responsiveness in inflammatory periodontal lesions.

L13 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:125795 CAPLUS
DOCUMENT NUMBER: 124:173266
TITLE: Cultured human Langerhans' cells are superior to fresh cells at presenting native HIV-1 protein antigens to specific CD4+ T-cell lines
AUTHOR(S): Girolomoni, G.; Valle, M. T.; Zacchi, V.; Costa, M. G.; Giannetti, A.; Manca, F.
CORPORATE SOURCE: Istituto Dermopatico dell'Immunacolata, IRCCS, Rome, Italy
SOURCE: Immunology (1996), 87(2), 310-16
CODEN: IMMUAM; ISSN: 0019-2805
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cultured Langerhans' cells (CLC) exhibit enhanced antigen-presenting function compared to freshly isolated LC (FLC), but they are commonly believed to be inefficient at processing intact proteins. In this study, FLC and CLC from normal, human immunodeficiency virus (HIV) seroneg.

volunteers were compared for their ability to present the HIV-1 envelope glycoprotein gp120 or reverse transcriptase (p66) antigens to autologous, specific **CD4**+ T cell lines. Epidermal cell suspensions enriched for LC were prepd. from suction blister roofs. FLC stimulated T cells at lower antigen concns. compared to unfractionated peripheral blood mononuclear cells (PBMC). CLC were more potent on a per cell basis than FLC, PBMC or adherent monocytes at presenting native gp120, native p66 or immunogenic peptides. CLC were also more efficient than FLC or PBMC in terms of the amt. of antigen required for T-cell activation. Chloroquine and leupeptin inhibited presentation of intact p66, but not of an immunodominant peptide, by FLC or CLC, thus indicating that both cells utilize antigen processing mechanisms that are based on intracellular acidification and protease activity. Incubation of CLC with monoclonal antibodies against HLA-DR, CD11b, CD18, **CD50**, **CD54**, CD58 or **CD80**, but not anti-major **histocompatibility** complex class I (MHC-I), inhibited antigen-specific T-cell proliferation to varying degrees. We conclude that human CLC retain the ability to process and present protein antigens potently to **CD4**+ T cells. Thus, CLC have the capacity to participate actively in the generation and maintenance of T-helper cell immunity to viral antigens during HIV-1 infection.

L13 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:122224 CAPLUS
DOCUMENT NUMBER: 124:200004
TITLE: Bone marrow-derived dendritic cell progenitors (NLDC 145+, MHC class II+, B7-1dim, B7-2-) induce alloantigen-specific hyporesponsiveness in murine T lymphocytes
AUTHOR(S): Lu, Lina; McCaslin, Delbert; Starzl, Thomas E.; Thomson, Angus W.
CORPORATE SOURCE: Pittsburgh Transplantation Institute, University Pittsburgh, Pittsburgh, PA, 15213, USA
SOURCE: Transplantation (**1995**), 60(12), 1539-45
CODEN: TRPLAU; ISSN: 0041-1337
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The functional maturation of dendritic cells (DC) and other antigen-presenting cells is believed to reflect the upregulation of cell surface major **histocompatibility** complex (MHC) class II and other T cell costimulatory mols., esp. the CD28 ligands **B7-1** (**CD80**) and B7-2 (CD86). In this study, we propagated cells exhibiting characteristics of DC precursors from the bone marrow (BM) of B10 mice (H-2b; I-A+) in response to granulocyte-macrophage colony stimulating factor (GM-CSF). The methods used were similar to those employed previously to propagate DC progenitors from normal mouse liver. Cells expressing DC lineage markers (NLDC 145+, 33D1+, N418+) harvested from 8-10-day GM-CSF stimulated BM cell cultures were **CD45**+, heat-stable antigen+, **CD54**+, **CD44**+, MHC class II+, B7-1dim but B7-2- (costimulatory mol.-deficient). Supplementation of cultures with interleukin-4 (IL-4) in addn. to GM-CSF however, resulted in marked upregulation of MHC class II and B7-2 expression. These latter cells exhibited potent allostimulatory activity in primary mixed leukocyte cultures. In contrast, the cells stimulated with GM-CSF alone were relatively weak stimulators and induced alloantigen-specific hyporesponsiveness in allogeneic T cells (C3H; H-2k; I-E+) detected upon restimulation in secondary MLR. This was assocd. with blockade of IL-2 prodn. Reactivity to third-party stimulators was intact. The hyporesponsiveness induced by the GM-CSF stimulated, costimulatory mol.-deficient cells was prevented by incorporation of anti-CD28 monoclonal antibody in the primary MLR and was reversed by addn. of IL-2 to restimulated T cells. The findings show that MHC class II+ B7-2- cells with a DC precursor phenotype can induce alloantigen-specific hyporesponsiveness in vitro. Under the appropriate conditions, such costimulatory mol.-deficient cells could contribute to the induction of donor-specific unresponsiveness in vivo.

L13 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:840493 CAPLUS
DOCUMENT NUMBER: 123:254196
TITLE: Differential effects of interleukin-10 on the expression of HLA class II and CD1 molecules induced by granulocyte/macrophage colony-stimulating factor/interleukin-4
AUTHOR(S): Thomssen, Henrike; Kahan, Melvyn; Londei, Marco
CORPORATE SOURCE: Kennedy Inst. Rheumatol., London, W6 8LW, UK
SOURCE: Eur. J. Immunol. (**1995**), 25(9), 2465-70
CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Interleukin (IL)-10 down-regulates HLA class II mols., whether constitutively expressed or up-regulated by interferon-.gamma. or IL-4 on monocytes but not on B lymphocytes. In this study the authors show that IL-10 does not inhibit HLA class II expression induced by the combination granulocyte/macrophage colony-stimulating factor and IL-4 on monocytes, although it simultaneously abrogates the expression of CD1 mols. induced by the same combination of cytokines. CD1 mols. can act as element of genetic restriction for **CD4**- CD8-T lymphocytes, and the suppression of CD1 expression by IL-10 abolished antigen presentation to CD1-restricted **CD4**- CD8-T cell receptor-pos. T cells. Although HLA class II expression was not down-regulated by IL-10, the antigen specific proliferative response of **CD4**+ T cells was nevertheless decreased. This was not caused by down-regulation of known co-stimulatory mols. such as **B7.1**, B7.2 and **ICAM**-1. IL-10 decreased the antigen specific proliferative response further by directly influencing the T lymphocytes. The results indicate that IL-10 exerts some of its immunoregulatory functions by differential modulation of antigen presenting mols., induced by the same combination of cytokines.

L13 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:820330 CAPLUS
DOCUMENT NUMBER: 123:225399
TITLE: The primary alloresponse of human **CD4**+ T cells is dependent on B7 (**CD80**), augmented by CD58, but relatively uninfluenced by **CD54** expression
AUTHOR(S): Hargreaves, Roseanna; Logiou, Vassiliki; Lechler, Robert
CORPORATE SOURCE: Department of Immunology, Royal Postgraduate Medical School, London, W12 0NN, UK
SOURCE: Int. Immunol. (**1995**), 7(9), 1505-13
CODEN: INIMEN; ISSN: 0953-8178
DOCUMENT TYPE: Journal

LANGUAGE: English
AB Conflicting data have been reported regarding the relative abilities of B7, **ICAM**-1 and LFA-3 to provide co-stimulation for the induction of a primary T cell alloproliferative response. A series of naturally HLA-DR-expressing cell lines and panels of human and murine transfectants expressing DR alloantigens in conjunction with combinations of mouse or human **B7.1**, human LFA-3 and human **ICAM**-1 were used to analyze the contributions of these mols. to primary alloproliferative responses by adult and cord blood **CD4**+ T cells. The results demonstrated that B7 expression is required, and may be sufficient for the induction of a primary alloresponse. The allostimulation obsd. in response to DR-expressing murine DAP.3 cells, that constitutively express **B7.1**, was inhibited by the presence of the murine cytolytic T lymphocyte-assocd. antigen 4-human Fc.gamma.1 fusion protein, suggesting that mouse **B7.1** provides sufficient co-stimulation for a primary human alloproliferative response. Expression of supranormal levels of human **B7**. **1** on the allostimulator cells led to a redn. in the proliferative response, suggesting that an optimal level of B7 exists which, if exceeded, leads to inhibition. Co-expression of LFA-3 with **B7**. **1** by the allostimulator cells caused a marked increase in the proliferative response. Expression of **ICAM**-1 had relatively little effect. No differences were seen in the co-stimulatory requirements of naive cord blood vs. **CD45RO** adult T cells. These results highlight the key mol. interactions that govern immunogenicity with relevance to inhibiting unwanted immune responses to transplanted tissues and providing anti-tumor immunity.

L13 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:766933 CAPLUS
DOCUMENT NUMBER: 123:167576
TITLE: Establishment of a cell line with features of early dendritic cell precursors from fetal mouse skin
AUTHOR(S): Girolomoni, Giampiero; Lutz, Manfred B.; Pastore, Saveria; Assmann, Caroline U.; Cavani, Andrea; Ricciardi-Castagnoli, Paola
CORPORATE SOURCE: Lab. of Immunology, Inst. Dermopatico dell'Immacolata, Rome, Italy
SOURCE: Eur. J. Immunol. (**1995**), 25(8), 2163-9
CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English
AB During ontogeny, the skin is progressively populated by major **histocompatibility** complex class II-neg. dendritic cell (DC) precursors that then mature into efficient antigen-presenting cells (APC). To characterize these DC progenitors better, we generated myeloid cell lines from fetal mouse skin by infecting cell suspensions with a retroviral vector carrying an envAKR-mycMH2 fusion gene. These cells, represented by the line FSDC, displayed a dendritic morphol. and their proliferation in serum-free medium was promoted by granulocyte/macrophage colony-stimulating factor (GM-CSF), but not by macrophage-CSF. FSDC expressed strong surface-membrane ATP/ADPase activity, intracellular staining for 2A1 antigen, and a surface phenotype consistent with a myeloid precursor: H-2d,b+, I-Ad,b+, **CD54**+, CD11b+, CD11c+, 2.4G2+, F4/80+, **CD44**+, 2F8+, ER-MP 12-, Sca-1+, Sca-2+, NLDC-145-, B7.2+, **B7**.,1-, J11d-, B220-, Thy-1-, and CD3-; FSDC stimulated poorly allogeneic or syngeneic T cells in the primary mixed-leukocyte reaction, and markedly increased this function after treatment with GM-CSF, GM-CSF and interleukin (IL)-4 or interferon-.gamma. (IFN-.gamma.); in contrast, stem cell factor, IL-1.alpha. and tumor necrosis factor-.alpha. had no effect. Preculture with IFN-.gamma. was required for presentation of haptens to primed T cells in vitro. However, FSDC, even after cytokine activation, were less potent APC than adult epidermal Langerhans cells in both of the above assays. Finally, FSDC derivatized with haptens and injected either i.v. or s.c. could efficiently induce contact sensitivity responses in naive syngeneic mice. The results indicate that fetal mouse skin is colonized by myeloid precursors possessing a macrophage/immature DC-like surface phenotype and priming capacity in vivo. These cells need further differentiation and activation signals (e.g. cytokines) to express their antigen presenting potential in vitro.

L13 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:757338 CAPLUS
DOCUMENT NUMBER: 123:225838
TITLE: CD86 (B70/B7-2) on endothelial cells co-stimulates allogeneic **CD4**+ T cells
AUTHOR(S): Seino, Kenichiro; Azuma, Miyuki; Bashuda, Hisashi; Fukao, Katashi; Yagita, Hideo; Okumura, Ko
CORPORATE SOURCE: Dep. Immunol., Juntendo Univ. Sch. Med., Bunkyo, 113, Japan
SOURCE: Int. Immunol. (**1995**), 7(8), 1331-7
CODEN: INIMEN; ISSN: 0953-8178
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In vascularized organ transplantation, vascular endothelial cells (EC) confronting recipient T cells are potentially significant APC initiating cellular immune responses that lead to rejection. In the present study, we studied the ability of human EC to stimulate allogeneic T cells and the co-stimulatory mols. involved in this response. On both human umbilical vein endothelial cells (HUVEC) and microvascular endothelial cells (MVEC), MHC class I, intercellular adhesion mol. (**ICAM**)-1 and CD86 were constitutively expressed as assessed by flow cytometry. After IFN-.gamma. treatment, MHC class II expression was induced, and MHC class I and **ICAM**-1 were up-regulated. In contrast, the expression of CD86 was unchanged and **CD80** was undetectable even after IFN-.gamma. treatment. Highly purified **CD4**+ T cells proliferated in response to IFN-.gamma.-treated allogeneic HUVEC and MVEC, and this response was efficiently blocked by mAb to MHC class II, **ICAM**-1 and CD86. Furthermore, the addn. of anti-CD86 mAb to the primary culture with allogeneic EC resulted in the induction of alloantigen-specific anergy. These results suggest that CD86 expressed on EC plays a crit. role in initiating cellular immune responses to vascularized allografts and would be an important target for immune intervention.

L13 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:692473 CAPLUS
DOCUMENT NUMBER: 123:109667
TITLE: Mechanism of enhanced antigen presentation by B cells activated with anti-.mu. plus interferon-.gamma.: role of B7-2 in the activation of naive and memory **CD4**+ T cells
AUTHOR(S): Morokata, Tatsuaki; Kato, Takuma; Igarashi, Osamu;

Nariuchi, Hideo
CORPORATE SOURCE: The Institute of Medical Science, The University of Tokyo, Tokyo, 108, Japan
SOURCE: Eur. J. Immunol. (1995), 25(7), 1992-8
CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English
AB B cells activated with anti-.mu. antibody plus interferon (IFN)-.gamma. exerted strong antigen presenting activity for T cell proliferation. The enhanced antigen presentation function was shown to be due to the increase in B7-2 expression. When B cells were stimulated with anti-.mu., expression of MHC major **histocompatibility** complex class II, heat-stable antigen (HSA), **ICAM**-1, and B7-2 was increased. The presence of IFN-.gamma. further augmented the expression of B7-2 on anti-.mu.-stimulated B cells. **B7-1** was not expressed on B cells under these conditions. The participation of B7-2 in the elicitation of the proliferative response of T cells was confirmed by the inclusion of anti-B7-2 antibody in cultures. The enhanced expression of either HSA or **ICAM**-1 was shown not to play a major role in the increased B cell antigen presentation capacity. The major T cell population responding to this activated B cell antigen presentation was shown to be **CD44low** naive **CD4**+ T cells, whereas **CD45RBlow** memory **CD4**+ T cells responded only weakly. The difference in proliferative responses between naive and memory **CD4**+ T cells was explained by the different efficiency in IL-2 prodn. of these cell populations in response to antigen presentation by B cells activated by anti-.mu. plus IFN-.gamma.. Thus, IFN-.gamma. plays an important role in recruitment of naive T cells for an immune response.

L13 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:633482 CAPLUS
DOCUMENT NUMBER: 123:31188
TITLE: Analysis of adhesion molecule-mediated signal transduction between T cells
AUTHOR(S): Wanibuchi, Masahiko; Murakami, Masaaki
CORPORATE SOURCE: Sch. Med., Sapporo Med. Univ., Japan
SOURCE: Sapporo Igaku Zasshi (1994), 63(5-6), 221-9
CODEN: SIZSAR; ISSN: 0036-472X
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB T cell activation requires engagement of the T cell receptor (TCR) with an immunogenic peptide bound to a major **histocompatibility** complex (MHC) mol. and a costimulatory signal provided by the antigen-presenting cell (APC). Although these events result in T cell clonal expansion, ligation of the TCR alone (lack of a costimulatory signal) does not stimulate T cell activation, but rather results in unresponsiveness known as T cell energy. Most investigations of the T cell activation mechanism have focussed on the system consisting of classical APC and T cells, but it is known that T cell can coexpress not only the adhesion mols. that provide costimulatory signals to T cells, but also their counter-receptors. In this paper, we analyze the role of adhesion mols. in T cell activation using a mouse **CD4**+ T cell clone, DB14. DB14 cells were able to proliferate upon stimulation of the TCR/CD3 complex alone either by appropriate MHC class II cDNA transfected CHO cells plus peptides or anti-CD3 monoclonal antibodies (mAb). Moreover the magnitude of anti-CD3 mAb-induced T cell proliferation was dependent on cell d., suggesting that cell to cell contact is important for the anti-CD3 mAb-induced DB cell proliferation. The DB14 cell expressed **B7-1**, CD28, **ICAM**-1 and LFA-1 mols. on its cell surface. Importantly, anti-CD3 mAb-induced proliferation was inhibited by CTLA-4 Ig or anti-LFA-1 mAb and the inhibitory effect of anti-LFA-1 mAb was stronger than that of CTLA-4 Ig. These results suggest that DB14 cells require two signals, the first, a TCR-mediated signal by anti-CD3 mAb and the second, a costimulatory signal through interaction of B7/CD28 and LFA-1/**ICAM**-1 pathways. Thus adhesion mols. on DB14 cells can provide a costimulatory signal for T cell proliferation, which suggests that T cells may provide costimulatory signals to each other at inflamed regions in vivo.

L13 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:609251 CAPLUS
DOCUMENT NUMBER: 123:31143
TITLE: Co-expression of **B7-1** and **ICAM**-1 on tumors is required for rejection and the establishment of a memory response
AUTHOR(S): Cavallo, Federica; Martin-Fontecha, Alfonso; Bellone, Matteo; Heltai, Silvia; Gatti, Evelina; Tornaghi, Paola; Freschi, Massimo; Forni, Guido; Dellabona, Paolo; Casorati, Giulia
CORPORATE SOURCE: CNR Immunogenetica e Oncologia Sperimentale, Universita di Torino, Italy
SOURCE: Eur. J. Immunol. (1995), 25(5), 1154-62
CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Although the transfection of **B7-1** cDNA into a few mouse tumor cell lines can induce anti-tumor T cell immunity, its expression alone is ineffective in many other tumor cell lines tested. We were interested to study what factors limit **B7-1** co-stimulatory activity, and decided to investigate whether **B7-1** requires the cooperation of **ICAM**-1 to provide the minimal co-stimulatory signal fro establishing an efficient anti-tumor immunity. We show that the transfection of **B7-1** cDNA into three **ICAM**-1+ (plasmacytoma J558L, T lymphomas EL-4 and RMA), but not into two **ICAM**-1- tumor cell lines (adenocarcinoma TS/A and melanoma B16.F1), is sufficient to induce their complete rejection in syngeneic mice. The expression of **ICAM**-1 is necessary for the rejection of the B7 expressing tumors, since the primary response elicited by **B7-1**+ EL-4 and RMA clones expressing reduced levels of **ICAM**-1 is severely reduced. Furthermore, super-transfection of **ICAM**-1 cDNA into **B7-1**+ adenocarcinoma and melanoma clones optimizes their primary rejection. **Histol**. examn. of transfected tumors reveals that **B7-1** and **ICAM**-1 exert a potent pro-inflammatory activity. The intra-tumor infiltration is composed of both eosinophils and lymphomonocytes, and is already massive 5 days after the tumor challenge. The primary rejection of the **B7-1**+**ICAM**-1+ tumors depends critically on CD8+ T cells, natural killer cells and granulocytes, but is independent of **CD4**+ T cells. Remarkably, in addn. to its effects on the early phases of the immune response, the co-expression of **ICAM**-1 and **B7-1** on tumors is also necessary for the efficient induction of a memory response. In fact, only the primary challenge with **B7**=

1+, ICAM-1+ tumor cells protects the majority of the mice from a second injection of parental tumor cells. Collectively, our findings indicate that B7-1 and ICAM-1 are fundamental components for triggering the primary injection of tumors and establishing a protective memory response. These findings may help to define new strategies for the rational application of co-stimulation in tumor immunotherapy.

L13 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:514551 CAPLUS
DOCUMENT NUMBER: 122:312753
TITLE: B7-1 expression decreases tumorigenicity and induces partial systemic immunity to murine neuroblastoma deficient in major histocompatibility complex and costimulatory molecules
AUTHOR(S): Katsanis, Emmanuel; Xu, Zhiyi; Bausero, Maria A.; Dancisak, Betsy B.; Gorden, Keith B.; Davis, Geoffrey; Gray, Gary S.; Orchard, Paul J.; Blazar, Bruce R.
CORPORATE SOURCE: Department of Pediatrics, University of Minnesota, Minneapolis, MN, USA
SOURCE: Cancer Gene Ther. (1995), 2(1), 39-46
CODEN: CGTHEG; ISSN: 0929-1903
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Neuroblastoma may escape an immune attack by virtue of its low expression of surface accessory mols. essential in the antitumor response. Murine neuroblastoma, neuro-2a, was transduced with the retroviral vector LB7-1SN to examine the influence of B7-1 expression on the immune response directed against a low major histocompatibility class (MHC) I and class II neg., B7-2, and ICAM-1 neg. tumor. Using a retroperitoneal model for implantation of neuroblastoma in its natural site, the authors demonstrated that expression of B7-1 by neuro-2a reduces its tumorigenicity. Coinjection of B7-1-pos. and -neg. cells improved survival compared with mice receiving B7-1-neg. cells alone. This was dependent on the ratio of B7-1+ to B7-1- neuro-2a cells injected. CD8+ and not CD4+ T-cell depletion significantly increased tumor-induced mortality in syngeneic A/J mice, indicating that B7-1 decreases tumorigenicity primarily by direct costimulation of CD8+ T cells. Rejection of N-2a/B7-1 tumors or preimmunization with irradiated N-2a/B7-1 cells did not increase protection to challenge with unmodified neuro-2a cells over mice vaccinated with N-2a/neo. Furthermore, cytotoxic T lymphocyte (CTL) precursor frequencies were not significantly higher after in vivo priming and in vitro stimulation with irradiated N-2a/B7-1 compared with N-2a/neo, indicating that B7-1 costimulation by the tumor, in the absence of adequate antigen presentation by MHC mols., may limit the generation of effective CTLs.

L13 ANSWER 15 OF 15 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:159793 BIOSIS
DOCUMENT NUMBER: PREV199799458996
TITLE: MHC class II-mediated antigen presentation by melanoma cells.
AUTHOR(S): Brady, Mary S. (1); Eckels, David D.; Ree, Sophia Y.; Schultheiss, Kim E.; Lee, Janet S.
CORPORATE SOURCE: (1) Memorial Sloan-Kettering Cancer Cent., 1275 York Avenue, New York, NY 10021 USA
SOURCE: Journal of Immunotherapy with Emphasis on Tumor Immunology, (1996) Vol. 19, No. 6, pp. 387-397.
ISSN: 1067-5582.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Constitutive expression of major histocompatibility complex (MHC) class II molecules is normally restricted to professional antigen-presenting cells (APCs) of the immune system, although it also occurs frequently in melanoma. Clinical evidence suggesting that MHC class II expression by melanoma is associated with tumor progression led us to postulate a role for MHC class II-mediated antigen presentation in this disease. First, we investigated whether melanoma cells derived from metastases can process antigen and/or present peptide vi MHC class II molecules to a peptide-specific CD4+ T-cell clone. In all cell lines tested, melanoma cells were able to process antigen and present peptide efficiently to CD4+ T cells, resulting in T-cell proliferation increased 5-26-fold over controls. Next, we found that CD28-mediated costimulation was not required, because blocking with CTLA4Ig had no effect on the T-cell response to either melanoma or B cells as APCs. In contrast, blocking CD54 (ICAM-1) resulted in a decrease in proliferation in response to peptide presentation by melanoma but not B cells. These data demonstrate that MHC class II molecules on melanoma cells are functional and that antigen-processing pathways are intact. In addition, CD54 seems to play a significant role in peptide presentation by melanoma.

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L1 14884 S WEBB S?/AU OR WINGVIST O?/AU OR KARLSSON L?/AU OR JACKSON M?/
L2 198 S L1 AND CD4?
L3 185 S L2 NOT CD40
L4 14 S L2 AND (CD80 OR B7.1)
L5 7 DUP REM L4 (7 DUPLICATES REMOVED)
L6 5 S L5 AND (ICAM? OR CD54 OR CD50 OR CD102)
L7 233993 S CD4?
L8 217789 S L7 NOT CD40
L9 2210 S L8 AND (CD80 OR B7.1)
L10 322 S L9 AND (ICAM? OR CD54 OR CD50 OR CD102)
L11 72 S L10 AND PD<19960523
L12 34 DUP REM L11 (38 DUPLICATES REMOVED)
L13 15 S L12 AND HIS?

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